UNIT –I

UNIT –II

UNIT –III

UNIT –IV

Nanotechnology

Nanotechnology ("nanotech") is manipulation of matter on an atomic, molecular, and supramolecular scale. The earliest, widespread description of nanotechnology referred to the particular technological goal of precisely manipulating atoms and molecules for fabrication of macroscale products, also now referred to as molecular nanotechnology. A more generalized description of nanotechnology was subsequently established by the National Nanotechnology Initiative, which defines nanotechnology as the manipulation of matter with at least one dimension sized from 1 to 100 nanometers.

Nanotechnology as defined by size is naturally very broad, including fields of science as diverse as surface science, organic chemistry, molecular biology, semiconductor physics, energy storage, microfabrication, molecular engineering, etc.

There are many different views of precisely what is included in nanotechnology. In general, however, most agree that three things are important:

- Small size, measured in 100s of nanometers or less
- Unique properties because of the small size
- Control the structure and composition on the nm scale in order to control the properties.

Nano system

Any physical system that is engineered at the nano scale.

Nanostructures

Objects with nanometer scale features are not new nor were they first created by man. There are many examples of nanostructures in nature in the way that plants and animals have evolved. Similarly there are many natural nanoscale materials catalysts, porous materials, certain minerals, soot particles, etc., that have unique properties particularly because of the nanoscale features. What is new about nanotechnology is that we can now, at least partially, understand and control these structures and properties to make new functional materials and devices. We have entered the era of engineered nanomaterials and devices.

Nanowires:

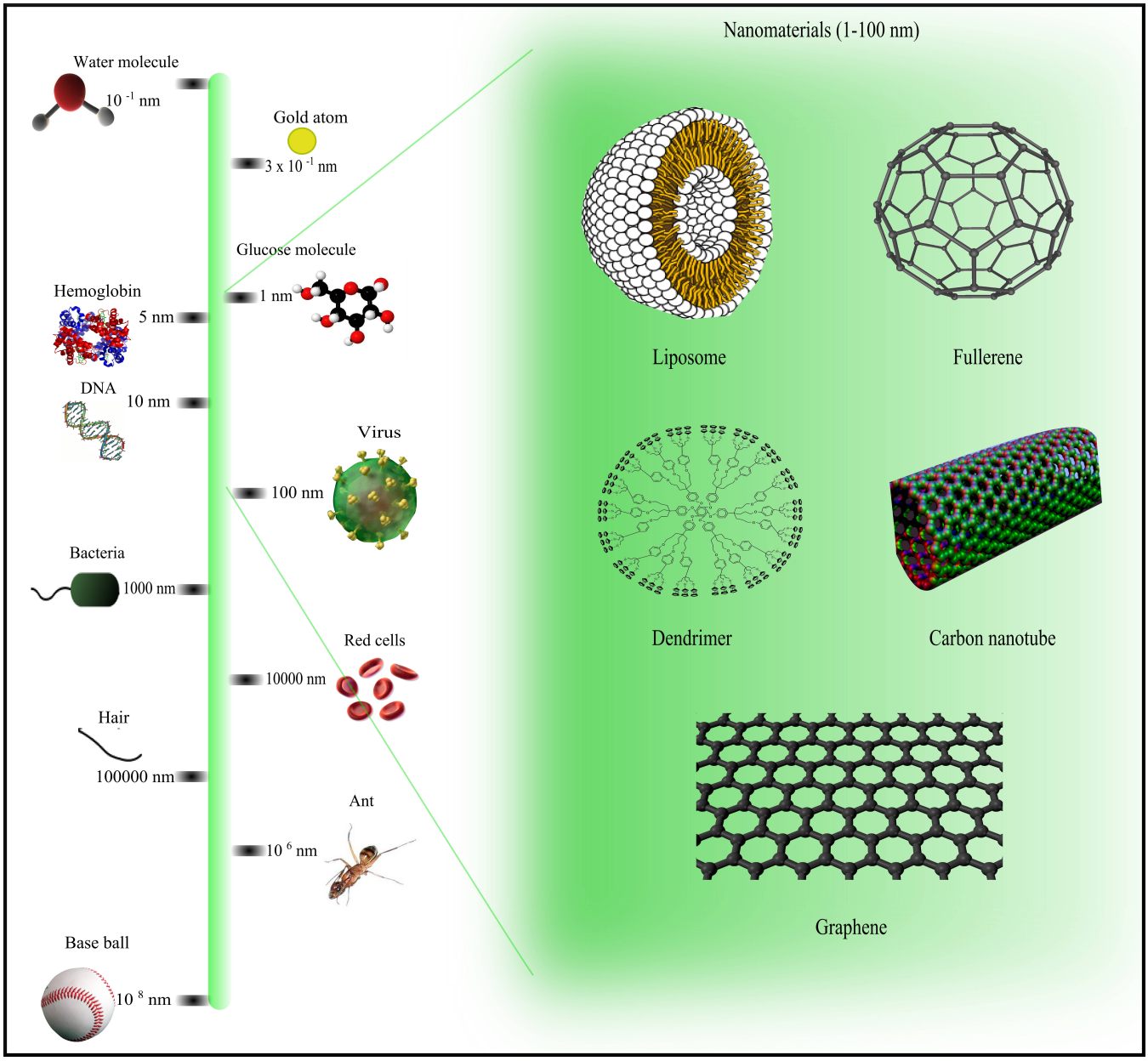
Nanowires are just like normal electrical wires other than the fact that they are extremely small. Like conventional wires, nanowires can be made from a variety of conducting and semiconducting materials like copper, silver, gold, iron, silicon, zinc oxide and germanium. Nanowires can also be made from carbon nanotubes.

Nanowire Size

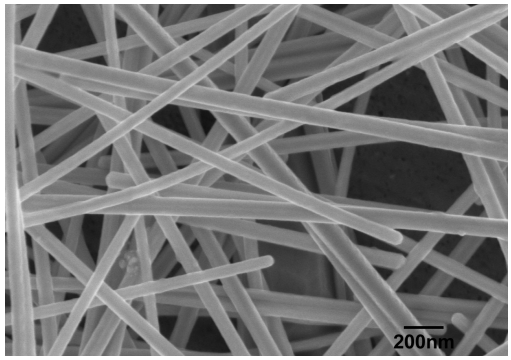
Nanowires are less than 100 nanometers in diameter and can be as small as 3 nanometers. Typically nanowires are more than 1000 times longer than their diameter. This massive difference in the length to diameter ratio means than nanowires are often referred to as 1-dimensional materials. This leads to unique properties that are not seen in the bulk materials, such as Quantum Mechanical Effects.

Quantum Mechanical Effects

The minute size of nanowires means that quantum mechanical effects become important. “Quantum Wires” exploit quantum mechanics to produce wires with a range of unique electrical properties. These properties include Quantum Tunnelling that allows wires made from carbon nanotubes to have extremely high conductivity with electrons travelling ballistically through the wire.


Nanomaterials (1-100 nm)
Water molecule
10 -1 nm
Gold atom
3 x 10 -1 nm
Glucose molecule
1 nm
Hemoglobin
5 nm
DNA
10 nm
Virus
100 nm
Bacteria
1000 nm
Red cells
10000 nm
Hair
100000 nm
Ant
10 6 nm
Base ball
10 8 nm
Liposome
Fullerene
Dendrimer
Carbon nanotube
Graphene

Nanowire Conductivity



Defects, edge effects and scattering caused when nanowire width is below the free electron mean free path of the wire material, means nanowires made from metals can have conductivity much lower than that for the bulk material.

Nanowires Applications

- Touch screens for smartphones, tablets, and wearable electronics
- Solar cells, solar panels, thin film photovoltaics
- Light-emitting diodes (LEDs), OLED devices, OLED lighting
- Liquid crystal displays
- Flexible displays
- e-paper
- Fillers for high performance conductive adhesives
- Surface enhanced spectroscopy (SERS)
- Sensors and detectors
- Air and water purification
- Medical imaging
- Antimicrobial applications (e.g., bandages, coatings for medical devices, antibacterial fabrics)
- Catalysts
- EMI shielding films and paints
- Optical limiters
- Flexible antennas
- Waveguides
- Compact logic gates

Quantum dot

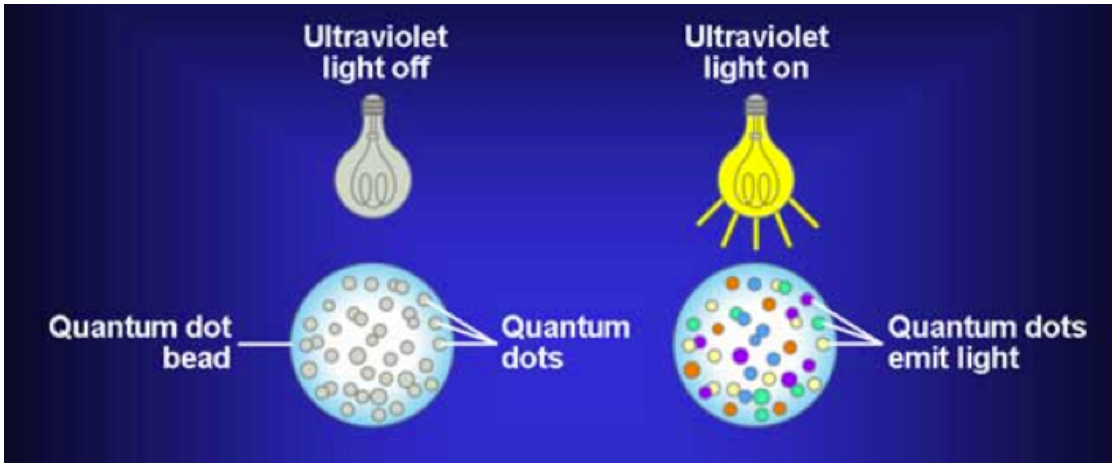
A quantum dot is a semiconductor nanostructure that confines the motion of conduction band electrons, valence band holes, or excitons (bound pairs of conduction band electrons and valence band holes) in all three spatial directions.

The confinement can be due to electrostatic potentials (generated by external electrodes, doping, strain, impurities), the presence of an interface between different semiconductor materials (e.g. in core-shell nanocrystal systems), the presence of the semiconductor surface (e.g. semiconductor nanocrystal), or a combination of these.

WHAT CAN WE DO WITH QUANTUM DOTS?

Quantum dots' ability to precisely convert and tune a spectrum of light makes them ideal for LCD displays. From smartphones to tablets to TVs, we can make all the colors we see even better by remixing white light into red, green and blue components. Until now, the white light that LCDs have had to work with wasn't very good, it contained a lot of blue and yellow but not very much red or green. This meant displays had to waste a lot of energy to make enough red and green for a bright display while also making for broad primary colors.

With quantum dots we can design an ideal spectrum of white light for an LCD, one that contains only the red, green and blue that the display needs to make a great image. The precise spectrum created by the dots makes colors pure. And since we're only making the colors the display needs we can use less power. The result is a display that's brighter, more power efficient and incredibly vibrant.



Dimensionality in nanomaterials

Nanomaterials can be classified in 0D, 1D, 2D and 3D nanomaterials. The dimensionality plays a major role in determining the characteristic of nanomaterials including physical, chemical and biological characteristics. With the decrease in dimensionality, an increase in surface-to-volume ratio is observed. This indicates that smaller dimensional nanomaterials have higher surface area compared to 3D nanomaterials. Recently, two dimensional (2D) nanomaterials are extensively investigated for electronic, biomedical, drug delivery and biosensor applications.

Nanowire

A nanowire is a wire of dimensions of the order of a nanometer (10−9 meters). Alternatively, nanowires can be defined as structures that have a lateral size constrained to tens of nanometers or less and an unconstrained longitudinal size. At these scales, quantum mechanical effects are important — hence such wires are also known as "quantum wires".

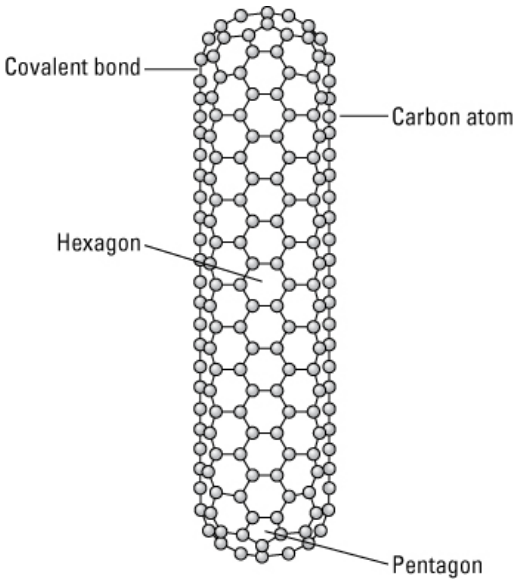
Many different types of nanowires exist, including metallic (e.g., Ni, Pt, Au), semiconducting (e.g., InP, Si, GaN, etc.), and insulating (e.g., SiO_2,TiO_2). Molecular nanowires are composed of repeating molecular units either organic or inorganic.

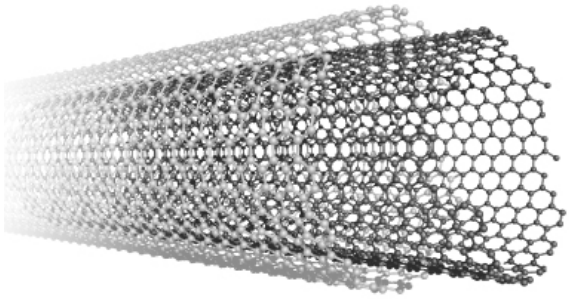
Nanotubes

A carbon nanotube is a tube-shaped material, made of carbon, having a diameter measuring on the nanometer scale. A nanometer is one-billionth of a meter, or about 10,000 times smaller than a human hair. CNT are unique because the bonding between the atoms is very strong and the tubes can have extreme aspect ratios. A carbon nanotube can be as thin as a few nanometers yet be as long as hundreds of microns. To put this into perspective, if your hair had the same aspect ratio, a single strand would be over 40 meters long.

The discovery of carbon nanotubes (CNT) in 1991 opened up a new era in materials science. These incredible structures have an array of fascinating electronic, magnetic and mechanical properties. CNT are at least 100 times stronger than steel, but only one-sixth as heavy, so nanotube fibers could strengthen almost any material. Nanotubes can conduct heat and electricity far better than copper. CNT are already being used in polymers to control or enhance conductivity and are added to anti-static packaging.

Carbon nanotubes have many structures, differing in length, thickness, and number of layers. The characteristics of nanotubes can be different depending on how the graphene sheet has rolled up to form the tube causing it to act either metallic or as a semiconductor. The graphite layer that makes up the nanotube looks like rolled-up chicken wire with a continuous unbroken hexagonal mesh and carbon molecules at the apexes of the hexagons.





2D Films

A new generation of nanoelectronic devices is emerging as a result of recent advances in research involving two-dimensional (2-D) nanomaterials.

The most widely studied 2-D nanomaterial is graphene, a single layer of carbon atoms only one molecule thick and packed in a hexagonal lattice. The material exhibits exceptional strength and possesses many other novel electrical and optical properties that have scientists buzzing since its first isolation in 2004. The electronic, thermal, and mechanical properties of graphene make it attractive for a variety of potential applications, including aerospace, automotive, electronics, energy storage, solar, oil service, and lubricant sectors.

However, graphene lacks one key property that has hampered development in electronic devices. Researchers have struggled to build electronic circuits out of graphene because the material lacks a bandgap, an important property that allows it to stop conducting or switch off, and is essential for many electronic applications.

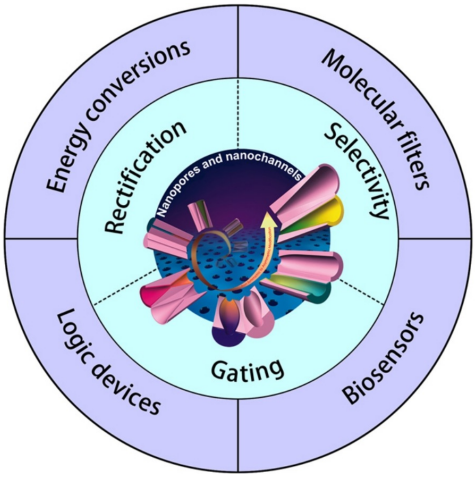
Molybdenum disulfide (MoS2), another 2-D nanomaterial, is proving to be much better suited for designing electronic components. MoS2 has been used as an industrial lubricant for decades, but a Swiss research team uncovered its 2-D potential in 2011 for creating highly flexible thin-film transistors.

Nanopores

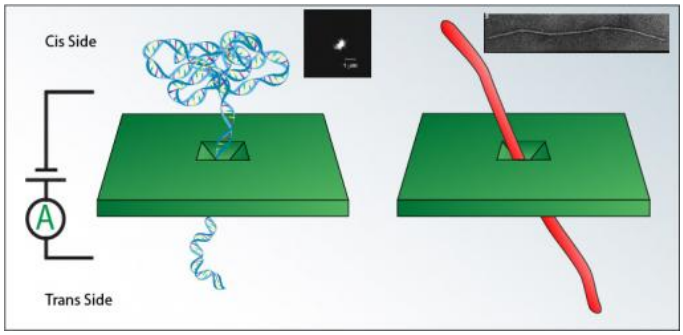
Nanopores are nanoscale pores in electrically insulating materials used to study the physical properties of biomolecules by measuring changes in current as individual molecules transit. Nanopore arrays are constructed from channel proteins in lipid membranes or from pores patterned in synthetic materials, and can sequence DNA or characterize protein folding.

Biological and protein nanopores

Nanopores may be formed by pore-forming proteins, typically a hollow core passing through a mushroom-shaped protein molecule. Examples of pore-forming proteins are alpha hemolysin and MspA porin. In typical laboratory nanopore experiments, a single protein nanopore is inserted into a lipid bilayer membrane and single-channel electrophysiology measurements are taken.

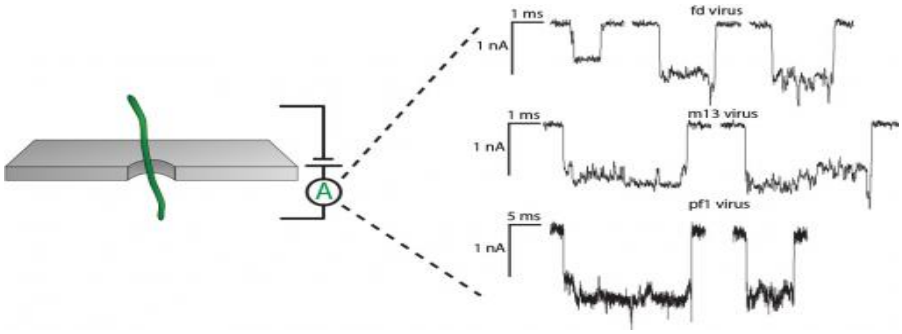


Nanopore studies of DNA and rod-like viruses



The qualitative differences in translocation due to differences in persistence length between DNA (left) and filamentous phage (right). The insets are a fluorescence microscopy image of a lambda DNA and an electron micrograph of an fd virus.

Nanopores of originally biological origin such as α-hemolysin, and later those made of solid-state materials, have been used to probe the structure and electro-physical properties of DNA. Nanopores are important from a technological standpoint because of their potential applications to DNA sequencing, as well as a unique tool to study polymer dynamics. My research involves studying the dynamics of DNA going through these small pores compared to much stiffer rod-like viruses. By measuring the current signals of these highly charged filamentous viruses as they are driven by an applied voltage to translocate through a solid-state nanopore, the fundamental physics of the process will be investigated. We hope that the results of the study will advance the development of nanopores as a sensor, leading to detection and discrimination of different filamentous viruses through the current blockage signal strength, duration, and other electrokinetic features to be defined. Completion of the project will lay the groundwork for a nanopore-based virus detection technology that could eventually result in cheap, throwaway, lab-on-a-chip type devices that transform molecular diagnostics.

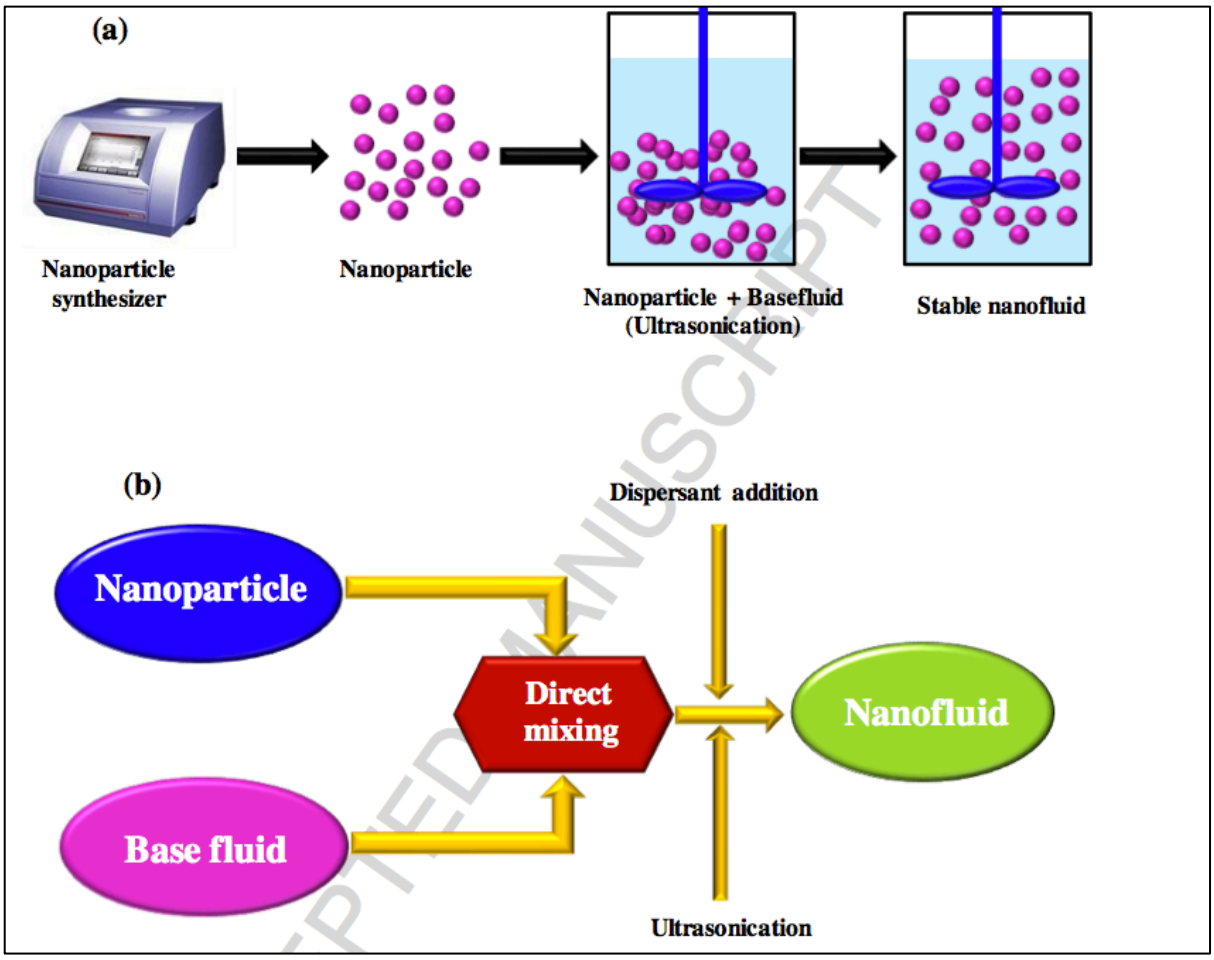


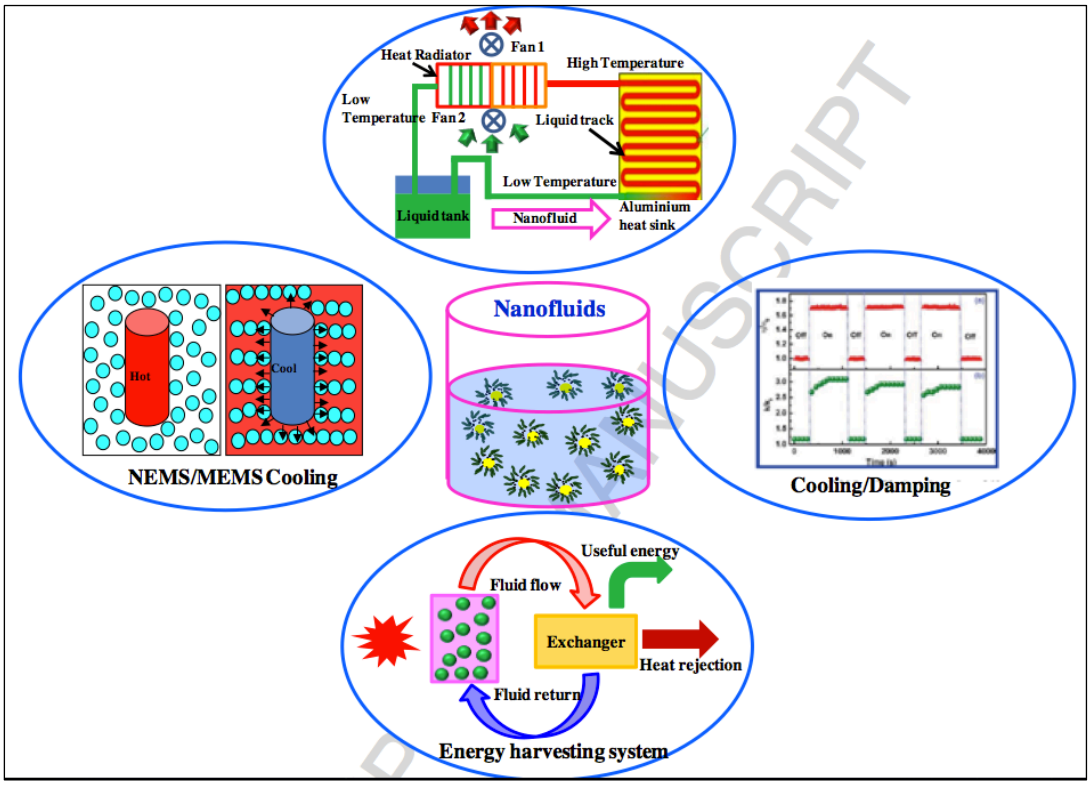
Nanofluid

A nanofluid is a fluid containing nanometer-sized particles, called nanoparticles. These fluids are engineered colloidal suspensions of nanoparticles in a base fluid. The nanoparticles used in nanofluids are typically made of metals, oxides, carbides, or carbon nanotubes. Common base fluids include water, ethylene glycol and oil.

Nanofluids have novel properties that make them potentially useful in many applications in heat transfer, including microelectronics, fuel cells, pharmaceutical processes, and hybrid-powered engines, engine cooling/vehicle thermal management, domestic refrigerator, chiller, heat exchanger, in grinding, machining and in boiler flue gas temperature reduction. They exhibit

enhanced thermal conductivity and the convective heat transfer coefficient compared to the base fluid. Knowledge of the rheological behaviour of nanofluids is found to be critical in deciding their suitability for convective heat transfer applications. Nanofluids also have special acoustical properties and in ultrasonic fields display additional shear-wave reconversion of an incident compressional wave; the effect becomes more pronounced as concentration increases.





NANO MATERIALS AND ITS PROPERTIES

Definition of NanoTechnology: Nanotechnology is the collaboration of the physics ,chemistry,biology,computer and material sciences integrated with engineering entering the nanoscale.This means science and engineering focused on making the particles,things and devices at the atomic and molecular scale.

Definition of Nano Particles: Nanomaterials or the Nanoparticles are the set of particles or the substances where atlas one dimension is less than approximately 100nm. or it can be also classically illustrated as the follows:

Nanomaterial is an object that has atleast one dimension in the nanometer scale approximately 1-100nm. Note: Richard Feynman is known as the father of nanotechnology.

Classification of the nanomaterials:

Due to the reduction in the spatial dimension, or confinement of particles or quasi particles in a particular crystallographic direction within a structure generally leads to changes in physical properties of the system in that direction. Hence classification of the nanostructured materials and systems essentially depends on the number of dimensions, which lie within the nanometer range.

a) Systems confined in 3 dimensions [Zero dimension structures] Examples: Nanoparticles; Nanograins; Nanoshells; Nanocapsules; Nanorings;Fullerenes;collidal particles; activatedcarbon; nanoporous silicon; quasi crystals.
b) Systems confined in 2 dimensions [One dimension structures] Examples: Nanorods; Nanofilaments; Nanotubes; quantum wires; nano wires.
c) Systems confined in 1 dimension. [two dimension structures] Examples: discs; platelets; ultrathin films; super lattices; quantum wells.

Magnetic properties:

Magnetic nanoparticles are used in a range of applications like imaging, bioprocessing,refrigeration as well as high storage density magnetic memory media. The large surface area to volume ratio results in a substantial proportion of atoms having different magnetic coupling with neighboring atoms leading to differing magnetic properties.

Bulk gold and platinum are non magnetic but at the nano size they act as magnetic particles.Au nanoparticles become ferromagnetic when they are capped with the appropriate molecules such as thiol.

Giant magnetoresistance(GMR) is a phenomenon observed in nanoscale multilayers consisting of strong ferromagnet (Fe,Co,Ni)and a weaker magnetic or non magnetic buffer(Cr,Cu).It is usually employed in data storage and sensing.

Optical properties:

In small nano clusters the effect of reduced dimensionality on electronic structure has the most profound effect on the energies of highest occupied molecular orbital (HOMO) which is valence band and the lowest unoccupied molecular orbital (LUMO),essentially the conduction band.

a) The optical emission and adsorption occurs when the transition of the electrons occur between these two states.

b) Semiconductors and many metals show large changes in optical properties such as color, as a function of particle size.
c) Colloidal suspenses of gold nano particles have a deep red color which becomes progressively more yellow as the particle size increases.
    - Gold spheres of 10-20nm exhibit red color
    - Gold spheres of 2-5nm exhibit yellow color
    - Gold spheres of >20nm exhibit purple color

Similarly,

- Silver particles of 40nm exhibit blue color
- Silver particles of 100nm exhibit yellow color
- Prism shaped Silver particles red color.

Other properties which may be affected by reduced dimensionality include photocatalysis, photoconductivity, photoemission and electroluminescence.

Electronic properties:

The changes which occur in electronic properties as the system length scale is reduced are related mainly to the increasing influence of the wave-like property of the electrons (quantum mechanical effects) and the scarcity of scattering centres.

As the size of the system becomes comparable with the de Broglie wavelength of the electrons, the discrete nature of the energy states becomes apparent once again, although a fully discrete energy spectrum is only observed in systems that are confined in all three dimensions.

In certain cases, conducting materials become insulators below a critical length scale, as the energy bands cease to overlap. Owing to their intrinsic wave-like nature, electrons can tunnel quantum mechanically between two closely adjacent nanostructures, and if a voltage is applied between two nanostructures which aligns the discrete energy levels in the DOS, resonant tunnelling occurs, which abruptly increases the tunnelling current.

Conduction in highly confined structures, such as quantum dots, is very sensitive to the presence of other charge carriers and hence the charge state of the dot. These Coulomb blockade effects result in conduction processes involving single electrons and as a result they require only a small amount of energy to operate a switch, transistor or memory element.

All these phenomena can be utilised to produce radically different types of compon- ents for electronic, optoelectronic and information processing applications, such as resonant tunnelling transistors and single-electron transistors.

Gold Nanoparticles - Properties, Applications

Introduction

For centuries gold has captivated mankind and has been considered as a precious metal. Reports state that colloidal gold nanoparticles have been utilized for centuries by artists for their vibrant colors, which are produced by their interaction with visible light. However, only in the 1850s scientists began studying their properties in more detail.

Gold is a Block D, Period 6 element. It is a soft metal that is often alloyed to give it more strength. It is a good conductor of heat and electricity. It is a good reflector of infrared and is chemically inert.

The versatile surface chemistry of gold nanoparticles allows them to be coated with small molecules, polymers, and biological recognition molecules, thereby extending their range of

application. The morphology of gold nanoparticles is spherical, and they appear as a brown powder.

Chemical Properties

The chemical properties of gold nanoparticles are outlined in the following table.

Chemical Data	
Chemical symbol	Au
CAS No.	7440-57-5
Group	11
Electronic configuration	[Xe] $4f^{142}$ $5d^{10}6s^1$

Physical Properties

The physical properties of gold nanoparticles are given in the following table.

Properties	**Metric**	**Imperial**
Density	19.30 g/cm^3	0.697 lb/in^3
Molar mass	196.97 g/mol	-

Thermal Properties

The thermal properties of gold nanoparticles are provided in the table below.

Properties	**Metric**	**Imperial**
Melting point	1064.43°C	1947.9741°F
Boiling point	2807°C	5084.6°F

Manufacturing Process

Gold nanoparticles are commonly produced in a liquid by reducing chloroauric acid. After dissolving the acid, the solution is rapidly mixed along with a reducing agent. This process then causes Au^{3+} ions to be reduced to neutral gold atoms.

As more of these gold atoms are generated, the solution becomes supersaturated. Gold then begins to precipitate in the form of sub-nanometer particles. If the solution is mixed in a vigorous manner, the particles tend to be uniform in size. A stabilizing agent is sometimes added to prevent the particles from aggregating.

Applications

Gold nanoparticles are versatile materials with a broad range of applications in a variety of fields. Researchers have coated gold particles with DNA and injected them into plant embryos or plant cells. This will ensure that some genetic material will enter the cells and transform them. This method enhances plant plastids.

The July 2007 issue of Analytical Chemistry reported that scientists from Purdue University were able to use gold nanoparticles to detect breast cancer. Later it was also discovered that the nanoparticles could detect toxins and pathogens.

The optical-electronics properties of gold nanoparticles are being explored widely for use in high technology applications such as sensory probes, electronic conductors, therapeutic agents, organic photovoltaics, drug delivery in biological and medical applications, and catalysis.

Other applications of gold nanoparticles are listed below:

- As an anti-biotic, anti-fungal, and anti-microbial agent when added in plastics, coatings, nanofibers and textiles
- In nanowires and catalyst applications
- In therapeutic agent delivery
- To connect resistors, conductors, and other elements of an electronic chip

- In photodynamic therapy - When light is applied to a tumor containing gold nanoparticles, the particles rapidly heat up, killing tumor cells
- In various sensors, e.g. colorimetric sensor with gold nanoparticles can identify if foods are suitable for consumption
- As substrates to enable the measurement of vibrational energies of chemical bonds in surface enhanced Raman spectroscopy
- The scattered colors of gold nanoparticles are currently used for biological imaging applications
- Gold nanoparticles are quite dense, thus allowing them to be used as probes for transmission electron microscopy
- To detect biomarkers in the diagnosis of cancers, heart diseases, and infectious agents
- As catalysts in a number of chemical reactions
- For fuel cell applications

Synthesis of Nanoparticles

Nanoparticles may be created using several methods. Some of them may occur in nature as well. The methods of creation include attrition and pyrolysis. While some methods are bottoms up, some are called top down. Top down methods involve braking the larger materials into nanoparticles.

Nanoparticle Synthesis	
Top-Down via	Bottom-Up via
Attrition / Milling	1) Pyrolysis 2) Inert gas condensation 3) Solvothermal reaction 4) Sol-Gel fabrication 5) Structured media

Attrition

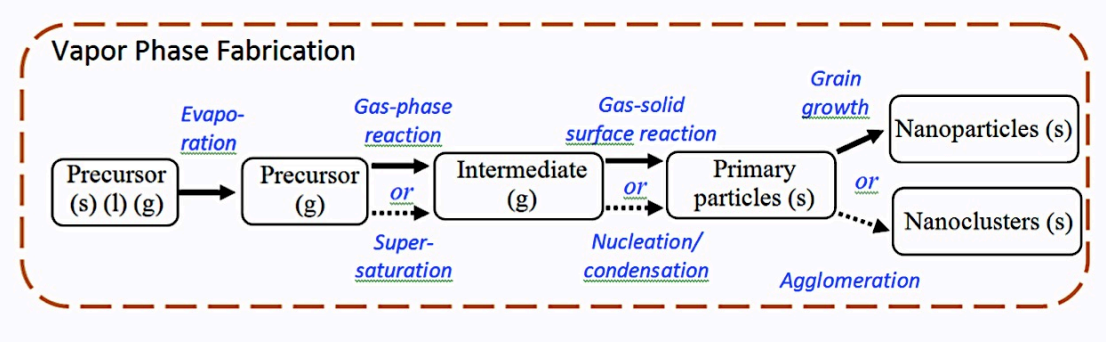
Attrition methods include methods by which macro or micro scale particles are ground in a ball mill, a planetary ball mill, or other size reducing mechanism. The resulting particles are air classified to recover nanoparticles.

- Involves mechanical thermal cycles
- Yields
  1. broad size distribution (10-1000 nm)
  2. varied particle shape or geometry
  3. impurities
- Application
  1) Nanocomposites
  2) Nano-grained bulk materials

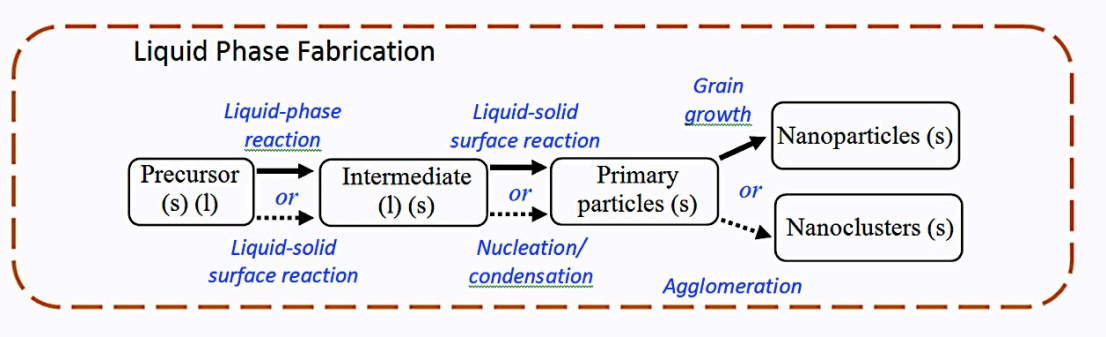
Bottoms up methods

These are further classified according to phases:

- Gas (Vapor) Phase Fabrication: Pyrolysis, Inert Gas Condensation



- Liquid Phase Fabrication: Solvothermal Reaction, Sol-gel, Micellar Structured Media



Pyrolysis

In pyrolysis, a vaporous precursor (liquid or gas) is forced through a hole or opening at high pressure and burned. The resulting solid is air classified to recover oxide particles from by-product gases. Pyrolysis often results in aggregates and agglomerates rather than singleton primary particles.

Instead of gas, thermal plasma can also deliver the energy necessary to cause evaporation of small micrometer size particles. The thermal plasma temperatures are in the order of 10,000 K, so that solid powder easily evaporates. Nanoparticles are formed upon cooling while exiting the plasma region. Examples of plasma used include dc plasma jet, dc arc plasma and radio frequency (RF) induction plasmas.

For example, silica sand can be vaporized with an arc plasma at atmospheric pressure. The resulting mixture of plasma gas and silica vapour can be rapidly cooled by quenching with oxygen, thus ensuring the quality of the fumed silica produced.

The advantages of vapor phase pyrolysis include it being a simple process, cost effective, a continuous operation with high yield.

Liquid phase synthesis methods

The liquid phase fabrication entails a wet chemistry route.
Methods are:

- Solvothermal Methods (e.g. hydrothermal)
- Sol-Gel Methods
- Synthesis in Structure Media (e.g., microemulsion)

Effectiveness of Solvothermal Methods and Sol-gel methods demands a simple process, low cost, continuous operation and high yield.

Solvothermal process

Precursors are dissolved in hot solvents (e.g., n-butyl alcohol) and solvent other than water can provide milder and friendlier reaction conditions If the solvent is water then the process is referred to as hydrothermal method.

Sol-gel process

The sol-gel process is a wet-chemical technique (also known as chemical solution deposition) widely used recently in the fields of materials science and ceramic engineering.
Steps include:

- Formation of stable sol solution
- Gelation via a polycondensation or polyesterification reaction
- Gel aging into a solid mass. This causes contraction of the gel network, also phase transformations and Ostwald ripening.
- Drying of the gel to remove liquid phases. This can lead to fundamental changes in the structure of the gel.
- Dehydration at temperatures as high as 8000 degree C, used to remove M-OH groups for stabilizing the gel, i.e., to protect it from rehydration.
- Densification and decomposition of the gels at high temperatures (T > 8000 degree C), i.e., to collapse the pores in the gel network and to drive out remaining organic contaminants

The ultimate microstructure of the final component will clearly be strongly influenced by changes implemented during this phase of processing. The precursor sol can be either deposited on a substrate to form a film (e.g. by dip-coating or spin-coating), cast into a suitable container with the desired shape (e.g. to obtain a monolithic ceramics, glasses, fibers, membranes, aerogels), or used to synthesize powders (e.g. microspheres, nanospheres).

Advantages of the sol-gel process

Advantages of the sol-gel process are that it is a cheap and low-temperature technique that allows for the fine control of the product's chemical composition. Even small quantities of dopants, such as organic dyes and rare earth metals, can be introduced in the sol and end up uniformly dispersed in the final product.

Characterization of nanoparticles:

Scanning Electron Microscopy (SEM)

This electron microscopy based technique determines the size, shape and surface morphology with direct visualization of the nanoparticles. Therefore scanning elec- tron microscopy offer several advantages in morphological and sizing analysis. However they provide limited information about the size distribution and true popu- lation average. During the process of SEM characterization, solution of nanoparti- cles should be initially converted into a dry powder. This dry powder is then further mounted on a sample holder followed by coating with a conductive metal (e.g. gold) using a sputter coater. Whole sample is then analyzed by scanning with a focused fine beam of electrons [20]. Secondary electrons emitted from the sample surface determine the surface characteristics of the sample. This electron beam can often damage the polymer of the nanoparticles which must be able to withstand vacuum. Average mean size evaluated by SEM is comparable with results obtained by dynamic light scattering. In addition

these techniques are time consuming, costly and frequently need complementary information about sizing distribution.

Transmission Electron Microscope

Experimental difficulties in studying nanostructures stem from their small size, which limits the use of traditional techniques for measuring their physical proper- ties. Transmission electron microscopy techniques can provide imaging, diffraction and spectroscopic information, either simultaneously or in a serial manner, of the specimen with an atomic or a sub-nanometer spatial resolution. TEM operates on different principle than SEM, yet it often brings same type of data. The sample preparation for TEM is complex and time consuming because of its requirement to be ultra thin for the electron transmittance. High-resolution TEM imaging, when combined with nanodiffraction, atomic resolution electron energy-loss spectros- copy and nanometer resolution X-ray energy dispersive spectroscopy techniques, is critical to the fundamental studies of importance to nanoscience and nanotechnol- ogy. During the TEM characterization nanoparticles dispersion is deposited onto support grids or films. After dispersion they are fixed using either a negative stain- ing material (phosphotungstic acid or derivatives, uranyl acetate, etc., or by plastic embedding). This is done to make nanoparticles withstand against the instrument vacuum and facilitate handling. Alternatively nanonoparticles sample can also be exposing to liquid nitrogen temperatures after embedding in vitreous ice. When a beam of electrons is transmitted through an ultra thin sample it interacts with the sample as it passes through The surface characteristics of the sample are obtained. TEM imaging mode has certain benefits compared with the broad-beam illu- mination mode:

- Collection of the information about the specimen using a high angular annular dark field (HAADF) detector (in which the images registered have different lev- els of contrast related to the chemical composition of the sample)
- It can be utilized for the analysis of biological samples is its contrast for thick stained sections, since high angular annular dark field images (samples with thickness of 100–120 nm) have better contrast than those obtained by other techniques.
- Combining HAADF-TEM imaging leads to imaging the atomistic structure and composition of nanostructures at a sub-angstrom resolution.
- Availability of sub-nanometer or sub-angstrom electron probes in a TEM instru- ment, due to the use of a field emission gun and aberration correctors, ensures the greatest capabilities for studies of sizes, shapes, defects, crystal and surface structures, and compositions and electronic states of nanometer-size regions of thin films, nanoparticles and nanoparticle systems.

Scanning probe microscopy

Scanning probe microscopy (SPM) is a widely used experimental technique for characterizing and fabricating nanostructures on surfaces. In particular, due to its ability to spatially map variations in materials properties with nanometer spatial resolution, SPM is particularly well suited to probe the subcomponents and interfaces of hybrid nanomaterials, i.e., materials that are made up of distinct nanometer scale components with distinguishable properties. In addition, the interaction of the SPM tip with materials can be intentionally tuned such that local surface modification is achieved. In this manner, hybrid nanostructures can also be fabricated on solid substrates using SPM.

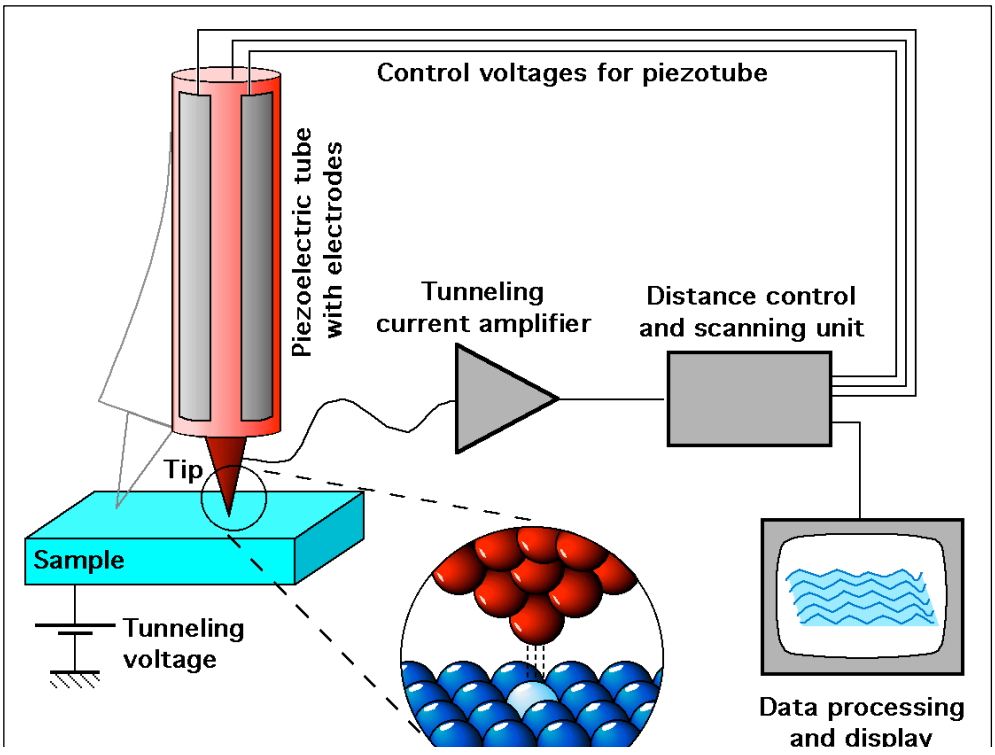
Atomic Force Microscopy

This technique is also known as scanning force microscopy (technique that forms images of surfaces using a prob that scans the specimen), very high resolution type of scanning probe microscopy, with reported resolution on the order of fractions of a nanomerter, more than 100 times better than the optical diffraction limit. The atomic force microscopy is based on a physical scanning of samples at sub-micron level using a probe tip of atomic scale and offers ultra-high resolution in particle size measurement. Depending upon properties, samples are usually scanned in contact or noncontact mode. During contact mode, the topographical map is gener- ated by tapping the probe on to the surface across the sample and probe hovers over the conducting surface in non-contact mode. One of the prime advantage of AFM is its ability to image non-conducting samples without any specific treatment. This feature allows the imaging of delicate biological and polymeric nano and micro- structures. Moreover AFM (without any mathematical calculation) provides the most accurate description of size, size distribution and real picture which helps in understanding the effect of various biological conditions.

scanning tunneling microscope

A **scanning tunneling microscope** (**STM**) is an instrument for imaging surfaces at the atomic level. Its development in 1981 earned its inventors, Gerd Binnig and Heinrich Rohrer (at IBM Zürich), the Nobel Prize in Physics in 1986. For a STM, good resolution is considered to be 0.1 nm lateral resolution and 0.01 nm (10 pm) depth resolution. With this resolution, individual atoms within materials are routinely imaged and manipulated. The STM can be used not only in ultra-high vacuum but also in air, water, and various other liquid or gas ambients, and at temperatures ranging from near zero kelvin to over 1000 °C.

STM is based on the concept of quantum tunneling. When a conducting tip is brought very near to the surface to be examined, a bias (voltage difference) applied between the two can allow electrons to tunnel through the vacuum between them. The resulting *tunneling current* is a function of tip position, applied voltage, and the local density of states (LDOS) of the sample. Information is acquired by monitoring the current as the tip's position scans across the surface, and is usually displayed in image form. STM can be a challenging technique, as it requires extremely clean and stable surfaces, sharp tips, excellent vibration control, and sophisticated electronics, but nonetheless many hobbyists have built their own.



Scanning nonlinear dielectric microscopy

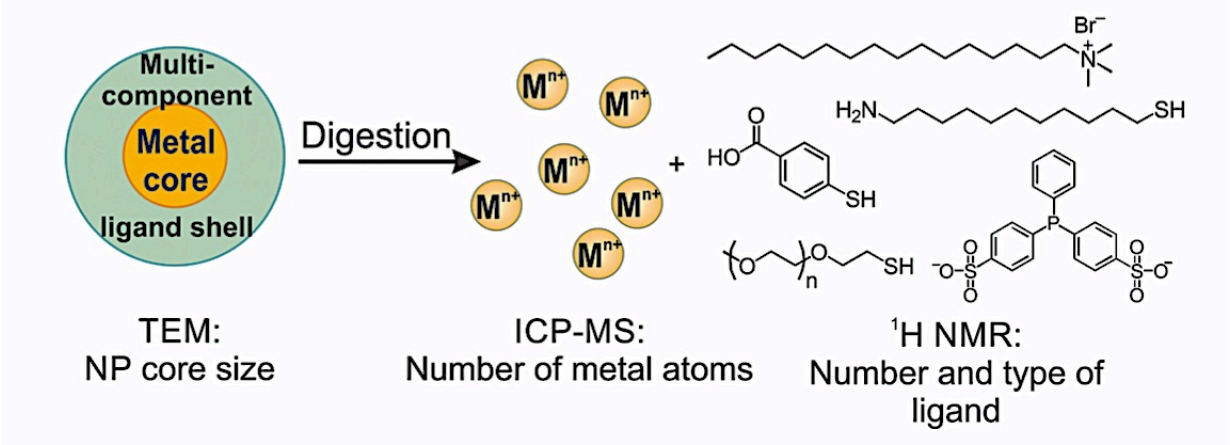
The new SNDM technique detecting higher nonlinear dielectric constants is . Higher order nonlinear

dielectric imaging provides higher lateral and depth resolution. Using this higher order nonlinear dielectric microscopy technique, the surface layer of ferroelectrics is investigated. A new type of scanning nonlinear dielectric microscope probe and a system to measure the ferroelectric polarization component parallel to the surface, are developed in the chapter. Scanning probe microscopy (SPM) is investigated as a method of forming and detecting small inverted domain dots in ferroelectric thin films such as lead zirconate titanate, or PZT (Pauch, Tybell, and Triscone). In this technique, domain dots are switched by applying a relatively large DC pulse to the probe, creating an electric field at the tip of the probe cantilever.

Nuclear magnetic resonance (NMR) spectroscopy

Nuclear magnetic resonance (NMR) spectroscopy is a transformational molecular characterization tool that requires little perturbation of the analyzed system, while providing exceptional detail about the chemical environments of constituent atomic nuclei. These features make NMR especially well-suited for in situ analysis of chemical structure, reactions, and even dynamics in some cases. With this versatility, it is not surprising that NMR analysis has been applied to a wide variety of systems1 ranging from large biomolecules2 to lithium batteries,3 in addition to its daily analytical use in organic synthesis laboratories. The chemical resolution possible using NMR is particularly attractive for characterizing both the formation and final architecture of noble metal nanoparticles (NMNPs). To understand why NMR is promising for these studies one must clarify both what one may want to determine about NMNP systems as well as the unique capabilities of NMR in metallic materials.

Analytical targets in the study of NMNPs range from tracking molecular precursors during NP formation to particle surface reorganization during catalytic reaction and many aspects of particle architecture, electronic properties, and surface chemistry in between. Nanoparticle systems often involve a hard–soft matter interface between the solid surface of the particle core and pendant ligands (species ranging from monoatomic ions to large macromolecules). This interface includes many parameters of interest including surface element composition, ligand shell composition, and ligand shell architecture. However, each of these features is difficult to resolve using classic surface and materials characterization strategies such as electron microscopy or photoelectron spectroscopy techniques.



Electron spin resonance

Rapid development of the nanoscience and technology has produced numerous nanomaterials that offer revolutionary benefits in electronics, energy, medical, and health applications, but unfortunately also lead to environmental, health, and safety concerns. For example, Au nanoparticles (NPs) have been explored as nanopharmaceuticals for the treat- ment

of cancer, and Ag NPs have been established as superior antibacterial materials. However, the wide use of nanomaterials has raised concerns regarding their potentially hazardous effects on biological systems, and the associated short- and long-term risks are not well under- stood. A variety of nanomaterials can generate reactive ox- ygen species (ROS) under certain experimental conditions. Among various toxic responses, nanomaterial- induced oxidative stress mediated by ROS has been studied most extensively.

ESR, also called electron paramagnetic resonance, is a powerful technique for studying chemical species or materials that have one or more unpaired electrons. The basic physical concepts of ESR are analogous to those of nuclear magnetic resonance, except that in ESR electron spins are excited instead of atomic nuclei. ESR has been studied for several decades since it was first observed by Y. Zavoisky in 1944. A number of review articles and books are available that provide a useful introduction to the basic concepts of ESR and its applications. An electron has a spin quantum number s =1/2 with magnetic components m_s = +1/2 and -1/2. In an external magnetic field, free electrons align with their spin parallel (low energy) or perpendicular (high energy) to the magnetic field. A transition between low- and high- energy states can occur when sufficient energy is absorbed. This energy lies within the microwave frequencies of the electromagnetic spectrum. The energy (hv) required for this transition is given by the following equation:

$$hv = g_e m_B B_0$$

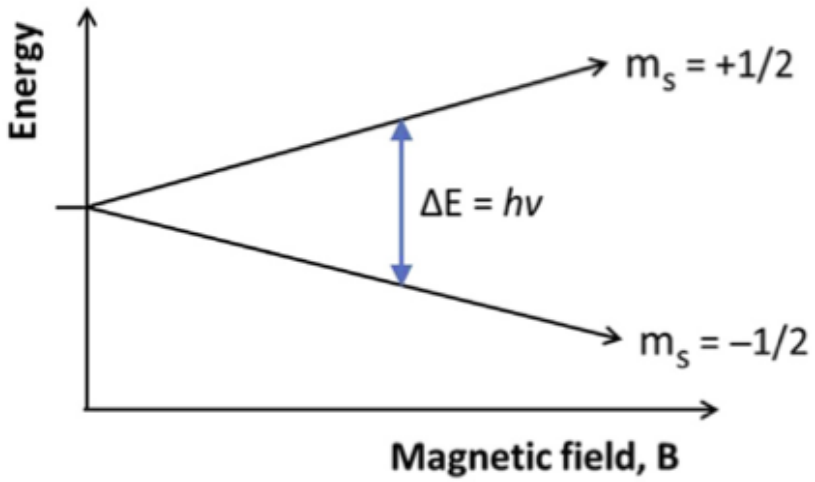


Fig. 1 – Energy diagram showing the origin of an ESR signal. ESR = electron spin resonance.

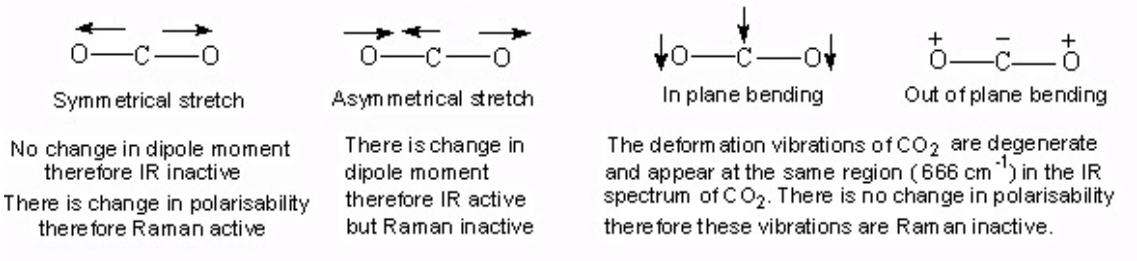
IR and Raman Spectroscopy

In a molecule with a center of symmetry it is seen that vibrations that are Raman active are IR inactive and vice-versa, this is called the Principle of mutual exclusion (eg, as in CO2 see details in the end). In molecules with different elements of symmetry, certain bands may be active in IR, Raman, both or neither. For a complex molecule that has no symmetry except identity element, all of the normal modes are active in both IR and Raman. This does not; however mean that they can be observed. In both types the neighbouring strong bands may obscure weak bands, while others may be intrinsically too weak to be observed even if they are theoretically “allowed”.

In general the strong bands in the IR spectrum of a compound corresponds to weak bands in the Raman and vice versa. This complimentary nature is due to the electrical characteristic of the vibration. If a bond is strongly polarised, a small change in its length such as that occurs during a vibration, will have only a small additional effect on polarisation. Vibrations involving polar bonds (C-O , N-O , O-H) are therefore, comparatively weak Raman scatterers. Such polarised bonds, however, carry their charges during the vibrational motion, (unless neutralised by symmetry factors), which results in a large net dipole moment change and produce strong IR absorption band. Conversely, relatively neutral bonds (C-C , C-H , C=C ,) suffer large changes in polarisability during a vibration, though this is less easy to visualise. But the dipole moment is not similarly affected and vibrations that predominantly involve this type of bond are strong Raman scatterers but weak in the IR.

Mutual exclusion principle as seen in CO_2

In molecules having inversion center, none of the normal modes of vibrations will be both Raman and IR active. This is known as "mutual exclusion principle". A simple molecule which obeys this principle is CO_2. Carbondioxide has an inversion center or center of symmetry. The following are its normal modes of vibrations. The IR and Raman active modes are indicated below each type of vibration.



Differences between IR and Raman methods

Raman	IR
It is due to the scattering of light by the vibrating molecules.	It is the result of absorption of light by vibrating molecules.
The vibration is Raman active if it causes a change in polarisability.	Vibration is IR active if there is change in dipole moment.
The molecule need not possess a permanent dipole moment.	The vibration concerned should have a change in dipole moment due to that vibration.
Water can be used as a solvent.	Water cannot be used due to its intense absorption of IR.
Sample preparation is not very elaborate, it can be in any state.	Sample preparation is elaborate Gaseous samples can rarely be used.
Gives an indication of covalent character in the molecule.	Gives an indication of ionic character in the molecule.
Cost of instrumentation is very high	Comparatively inexpensive.

UNIT -V

Nanotechnology Applications:

Medicine: Researchers are developing customized nanoparticles the size of molecules that can deliver drugs directly to diseased cells in your body. When it's perfected, this method should greatly reduce the damage treatment such as chemotherapy does to a patient's healthy cells.

Electronics: Nanotechnology holds some answers for how we might increase the capabilities of electronics devices while we reduce their weight and power consumption.

Food: Nanotechnology is having an impact on several aspects of food science, from how food is grown to how it is packaged. Companies are developing nanomaterials that will make a difference not only in the taste of food, but also in food safety, and the health benefits that food delivers.

Fuel Cells: Nanotechnology is being used to reduce the cost of catalysts used in fuel cells to produce hydrogen ions from fuel such as methanol and to improve the efficiency of membranes used in fuel cells to separate hydrogen ions from other gases such as oxygen.

Solar Cells: Companies have developed nanotech solar cells that can be manufactured at significantly lower cost than conventional solar cells.

Batteries: Companies are currently developing batteries using nanomaterials. One such battery will be a good as new after sitting on the shelf for decades. Another battery can be recharged significantly faster than conventional batteries.

Space: Nanotechnology may hold the key to making space-flight more practical. Advancements in nanomaterials make lightweight spacecraft and a cable for the space elevator possible. By significantly reducing the amount of rocket fuel required, these advances could lower the cost of reaching orbit and traveling in space.

Fuels: Nanotechnology can address the shortage of fossil fuels such as diesel and gasoline by making the production of fuels from low grade raw materials economical, increasing the mileage of engines, and making the production of fuels from normal raw materials more efficient.

Better Air Quality: Nanotechnology can improve the performance of catalysts used to transform vapors escaping from cars or industrial plants into harmless gasses. That's because catalysts made from nanoparticles have a greater surface area to interact with the reacting chemicals than catalysts made from larger particles. The larger surface area allows more chemicals to interact with the catalyst simultaneously, which makes the catalyst more effective.

Cleaner Water: Nanotechnology is being used to develop solutions to three very different problems in water quality. One challenge is the removal of industrial wastes, such as a cleaning solvent called TCE, from groundwater. Nanoparticles can be used to convert the contaminating chemical through a chemical reaction to make it harmless. Studies have shown that this method can be used successfully to reach contaminates dispersed in underground ponds and at much lower cost than methods which require pumping the water out of the ground for treatment.

Chemical Sensors: Nanotechnology can enable sensors to detect very small amounts of chemical vapors. Various types of detecting elements, such as carbon nanotubes, zinc oxide nanowires or palladium nanoparticles can be used in nanotechnology-based sensors. Because of the small size of nanotubes,

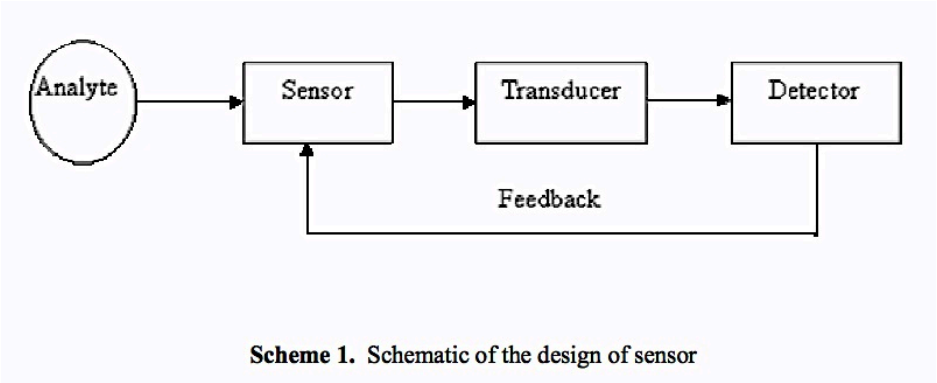
nanowires, or nanoparticles, a few gas molecules are sufficient to change the electrical properties of the sensing elements. This allows the detection of a very low concentration of chemical vapors.

Fabric: Making composite fabric with nano-sized particles or fibers allows improvement of fabric properties without a significant increase in weight, thickness, or stiffness as might have been the case with previously-used techniques.

Nanosensors

Nanosensors are chemical or mechanical sensors that can be used to detect the presence of chemical species and nanoparticles, or monitor physical parameters such as temperature, on the nanoscale. They also find use in medical diagnostic applications.

Our modern lives rely on sensors to allow society to run smoothly. Sensors in the road detect cars at traffic lights and adjust the flow through intersections accordingly. Sensors at shopping malls detect your presence and open doors to allow you to enter. Sensors measure the water level in your washing machine and ensure it doesn't overflow.



Scheme 1. Schematic of the design of sensor

Nanosensors work in much the same way but they can detect either minute particles or miniscule quantities of something.

Types of sensors

- Ultrasonic sensors
- Infrared sensors
- Piezoelectric sensors
- Gas sensors
- Magnetoelectric sensors
- Biosensors

Types of sensors (Classification on the measured parameter)

- Pressure
- Flow sensors
- Level
- Temperatures
- Sensor concentration
- Radioactivity
- Move
- Terms
- Photosensors
- Angular position sensor
- Vibration sensor
- Sensor mechanical quantities
- Sensor arc protection

Classification on the basis of actions:

- Optical sensors (photocells)
- Moving coil sensor (Hall effect)
- The piezoelectric sensor
- Load cells
- Capacitive sensor
- Based sensors
- Inductive

Nanosensor Applications

Nanosensors can be chemical sensors or mechanical sensors. Amongst other applications they can be used:

- To detect various chemicals in gases for pollution monitoring

- For medical diagnostic purposes either as blood borne sensors or in lab-on-a-chip type devices
- To monitor physical parameters such as temperature, displacement and flow
- As accelerometers in MEMS devices like airbag sensors
- Military-space complex
- Comforts of home

Chemical Nanosensors

Typically nanosensors work by monitoring electrical changes in the sensor materials. Carbon nanotube based sensors work in this way. For instance when a molecule of nitrogen dioxide (NO2) is present it will strip an electron from the nanotube, which in turn causes the nanotube to be less conductive. If ammonia (NO3) is present it reacts with water vapour and donates an electron to the carbon nanotube, making it more conductive. By treating the nanotubes with various coating materials, they can be made sensitive to certain molecules and immune to others.

Mechanical Nanosensors

Like chemical nanosensors, mechanical nanosensors also tend to measure electrical changes. The nanosensors used in the MEMS systems that car airbags depend upon are monitoring changes in capacitance. These systems have a miniscule weighted shaft attached to a capacitor. The shaft bends with changes in acceleration and this is measured as changes in capacitance.

Nanocarriers

A nanocarrier is nanomaterial being used as a transport module for another substance, such as a drug. Commonly used nanocarriers include micelles, polymers, carbon-based materials, liposomes and other substances. Nanocarriers are currently being studied for their use in drug delivery and their unique characteristics demonstrate potential use in chemotherapy.

Characterization

Nanocarriers range from sizes of diameter 1–1000 nm, however due to the width of microcapillaries being 200 nm, nanomedicine often refers to devices <200 nm. Because of their small size, nanocarriers can deliver drugs to otherwise inaccessible sites around the body. Since nanocarriers are so small, it is oftentimes difficult to provide large drug doses using them. The emulsion techniques used to make nanocarriers also often result in low drug loading and drug encapsulation, providing a difficulty for the clinical use.

Types

Nanocarriers discovered polymer conjugates, polymeric nanoparticles, lipid-based carriers, dendrimers, carbon nanotubes, and gold nanoparticles. Lipid-based carriers include both liposomes and micelles. Examples of gold nanoparticles are gold nanoshells and nanocages. Different types of nanomaterial being used in nanocarriers allows for hydrophobic and hydrophilic drugs to be delivered throughout the body. Since the human body contains mostly water, the ability to deliver hydrophobic drugs effectively in humans is a major therapeutic benefit of nanocarriers. Micelles are able to contain either hydrophilic or hydrophobic drugs depending on the orientation of the phospholipid molecules. Some nanocarriers contain nanotube arrays allowing them to contain both hydrophobic and hydrophilic drugs.

Targeted drug delivery

Nanocarriers are useful in the drug delivery process because they can deliver drugs to site-specific targets, allowing drugs to be delivered in certain organs or cells but not in others. Site-specificity is a major therapeutic benefit since it prevents drugs from being delivered to the wrong places. Nanocarriers show promise for use in chemotherapy because they can help decrease the adverse, broader-scale toxicity of chemotherapy on healthy, fast growing cells around the body. Since

chemotherapy drugs can be extremely toxic to human cells, it is important that they are delivered to the tumor without being released into other parts of the body. Four methods in which nanocarriers can deliver drugs include passive targeting, active targeting, pH specificity, and temperature specificity.

Passive targeting

Passive targeting refers to a nanocarrier's ability to travel down a tumor's vascular system, become trapped, and accumulate in the tumor. This accumulation is caused by the enhanced permeability and retention effect which refers to the poly(ethylene oxide) (PEO) coating on the outside of many nanocarriers. PEO allows nanocarriers to travel through the leaky vasculature of a tumor, where they are unable to escape. The leaky vasculature of a tumor is the network of blood vessels that form in a tumor, which contain many small pores. These pores allow nanocarriers in, but also contain many bends that allow the nanocarriers to become trapped. As more nanocarriers become trapped, the drug accumulates at the tumor site. This accumulation cause large doses of the drug to be delivered directly to the tumor site. PEO may also have some adverse effects on cell-nanocarrier interactions, weakening the effects of the drug, since many nanocarriers must be incorporated into the cells before the drugs can be released.

Active targeting

Active targeting involves the incorporation of targeting modules such as ligands or antibodies on the surface of nanocarriers that are specific to certain types of cells around the body. Nanocarriers have such a high surface-area to volume ratio allowing for multiple ligands to be incorporated on their surfaces. These targeting modules allow for the nanocarriers to be incorporated directly inside of cells, but also have some drawbacks. Ligands may cause nanocarriers to become slightly more toxic due to non-specific binding, and positive charges on ligands may decrease drug delivery efficiency once inside of cells. Active targeting has been shown to help overcome multi-drug resistance in tumor cells.

pH specificity

Certain nanocarriers will only release the drugs they contain in specific pH ranges. pH specificity also allows nanocarriers to deliver drugs directly to a tumor site. Tumors are generally more acidic than normal human cells, with a pH around 6.8. Normal tissue has a pH of around 7.4. Nanocarriers that only release drugs at certain pH ranges can therefore be used to release the drug only within acidic tumor environments. High acidic environments cause the drug to be released due to the acidic environment degrading the structure of the nanocarrier. These nanocarriers will not release drugs in neutral or basic environments, effectively targeting the acidic environments of tumors while leaving normal body cells untouched. This pH sensitivity can also be induced in micelle systems by adding copolymer chains to micelles that have been determined to act in a pH independent manor. These micelle-polymer complexes also help to prevent cancer cells from developing multi-drug resistance. The low pH environment triggers a quick release of the micelle polymers, causing a majority of the drug to be released at once, rather than gradually like other drug treatments. This quick release mechanism significantly decreases the time it takes for anticancer drugs to kill a tumor, effectively preventing the tumor from having time to undergo mutations that would render it drug resistant.

Temperature specificity

Some nanocarriers have also been shown to deliver drugs more effectively at certain temperatures. Since tumor temperatures are generally higher than temperatures throughout the rest of the body, around 40 °C, this temperature gradient helps act as safeguard for tumor-specific site delivery.

Nanocarriers And Drug Delivery

Biomaterials are useful in drug delivery and targeting, since they can be optimized as controlled release formulations and also as nanoparticles for intracellular drug delivery. Our unique

interdisciplinary research program couples both physico-chemical and biological aspects in this area. The research is focused in particular on continuous protein delivery from microencapsulated cells and on nanoparticle-mediated gene delivery and targeted anti-cancer drug research.

Research perform experiment with nanoparticulate systems with the aim of better understanding the delivery process. Packing of pDNA with polycations is used to form DNA nanoparticles, but structural features of the resulting nanoparticulates are poorly understood. A new time-resolved spectroscopic method was established for DNA packing studies. The method revealed interesting differences between PLL- and PEI-DNA complexes; the latter shows tightly bound and mobile DNA, whereas PLL-DNA complexes have only tightly bound DNA. The mobile PEI-based complexes have about 100-fold higher activity of transfection per DNA copy delivered to the cell nucleus. We have also demonstrated that the interactions of free PEI with cell surface glycosaminoglycans (GAG) improve DNA transfection, presumably by a decoy effect that reduces the interactions between the complexes and GAGs. We also performed a careful mechanistic study to investigate cell penetrating peptides that have been claimed to permeate directly through the cell membrane. In contrast to published reports, we did not observe this. All TAT-peptide variants were endocytosed and trapped within endosomal and lysosomal vesicles.

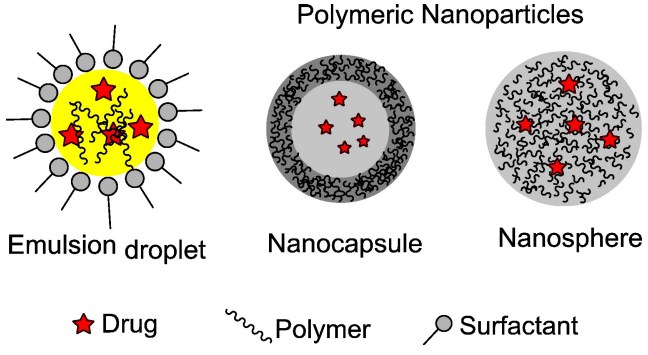
Polymeric nanoparticles

Polymeric nanoparticles (PNPs) have attracted considerable interest over the last few years due to their unique properties and behaviors resulting from their small size. Asasserted by different authors, these nanoparticulate materials show potential for a wide range of applications such as diagnostics and drug delivery. Advantages of PNPs as carriers include controlled release, the ability to combine both, therapy and imaging (theranostics), protection of drug molecules and its specific targeting, facilitating improvements in the therapeutic index.

The uptake of nanoparticles into cells usually involves endocytotic processes, which depend primarily on their size and surface characteristics. These properties can be tuned by the nanoparticle preparation method. Depending upon the preparation method and composition of the organic phase, nanocapsules or nanospheres can be obtained. A nanocapsule particle has core-shell morphology with an aqueous or oily cavity in which the active compounds are confined and surrounded by a polymer shell. Nanospheres have a matrix-like structure in which the active compounds and the polymer are uniformly dispersed.

Effective post-synthesis purification of nanoparticles is also an important step for controlling their quality and characteristics and therefore their suitability for a biomedical application. Depending on the preparation method, several impurities will be present in the nanoparticle suspension and adsorbed to the nanoparticles. These potentially toxic impurities include organic solvents, salts, particle aggregates, and reagent residues. Filtration, centrifugation and dialysis techniques are commonly used purification methods.

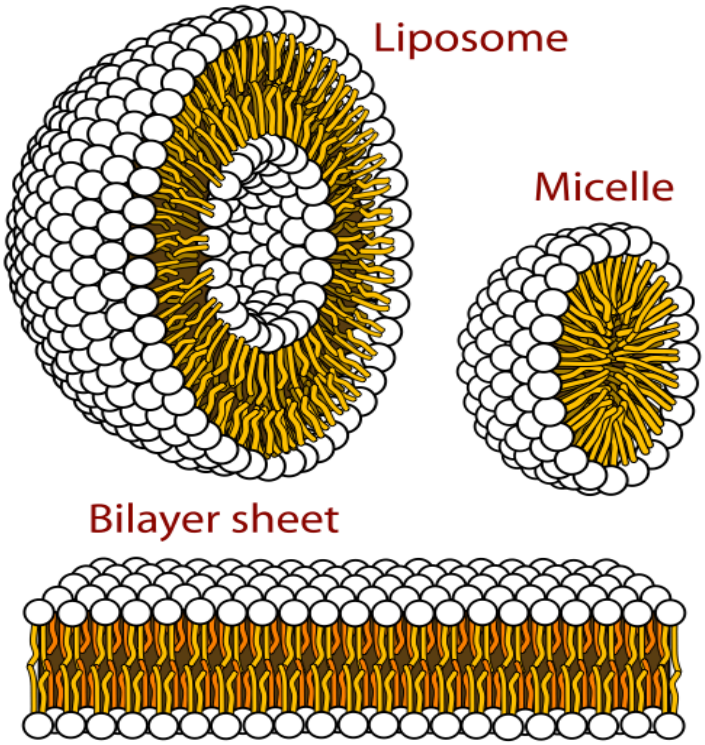
Herein the preparation techniques and characterization of PNPs are reviewed. The aim is to collect and compile the information, and also to update and highlight recent developments. We hope the information covered in this review will stimulate the development of novel nanomedicines that are easier to handle, compatible with physiological media and suitable for further clinical developments.



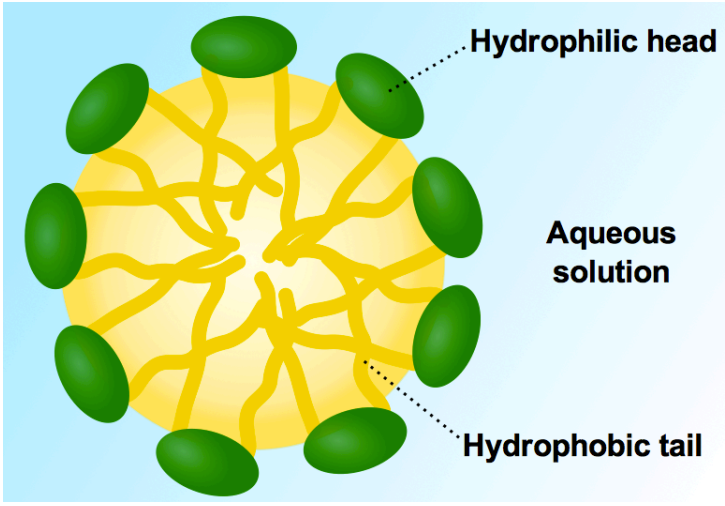
Micelle

A micelle (/maɪˈsɛl/) or micella (/maɪˈsɛlə/) (plural micelles or micellae, respectively) is an aggregate (or supramolecular assembly) of surfactant molecules dispersed in a liquid colloid. A typical micelle in aqueous solution forms an aggregate with the hydrophilic "head" regions in contact with

surrounding solvent, sequestering the hydrophobic single-tail regions in the micelle centre. This phase is caused by the packing behavior of single-tail lipids in a bilayer. The difficulty filling all the volume of the interior of a bilayer, while accommodating the area per head group forced on the molecule by the hydration of the lipid head group, leads to the formation of the micelle. This type of micelle is known as a normal-phase micelle (oil-in-water micelle). Inverse micelles have the head groups at the centre with the tails extending out (water-in-oil micelle). Micelles are approximately spherical in shape. Other phases, including shapes such as ellipsoids, cylinders, and bilayers, are also possible. The shape and size of a micelle are a function of the molecular geometry of its surfactant molecules and solution conditions such as surfactant concentration, temperature, pH, and ionic strength. The process of forming micelles is known as micellisation and forms part of the phase behaviour of many lipids according to their polymorphism.



Phospholipids aqueous solution structures



Micelle scheme

Background

Thermogels are polymers that are liquid when refrigerated and solid when at room temperature. The polymer's steric hindrance combined with a low molecular weight prevents crystallization, and therefore creates thermosensitivity.

PolySciTech's PolyVivo line offers these non-crystaline thermogel polymers in a wide variety of products. We are sure to have one just to your liking. PolyVivo polymers can be purchased at PolySciTech.com. If, however, you cannot find a thermogel for your needs, we do offer custom synthesis.

Why thermogel?

Micelle-type structure improves hydrophobic drug solubility and aids microparticle dispersion In-vivo and in-vitro applications

Injectable
Degradable

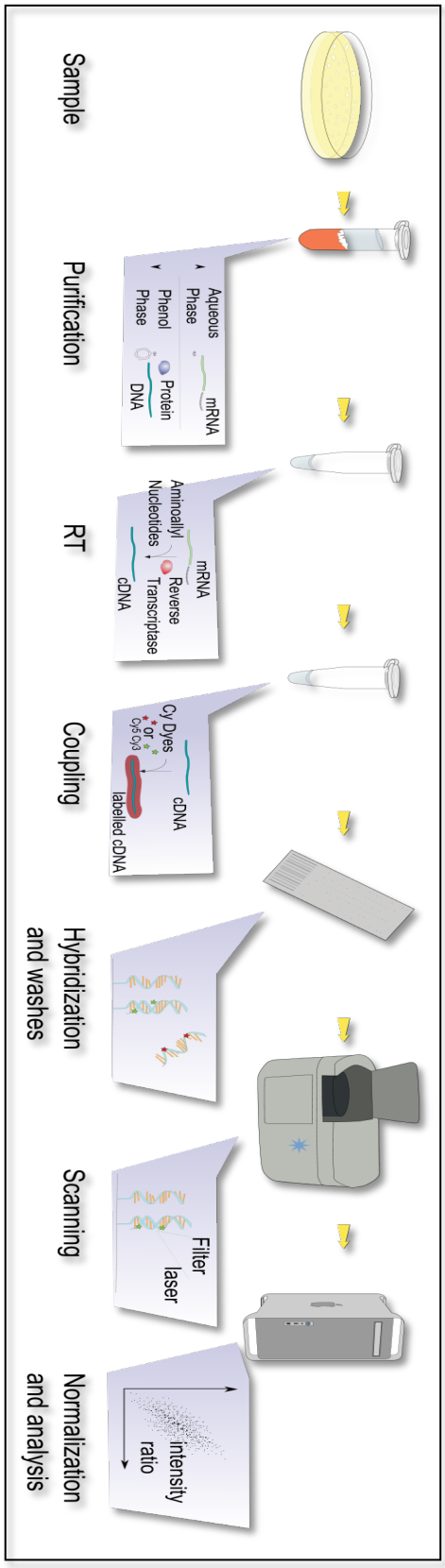
Properties

Extremely sticky and viscous in its dry and natural state
Polymers thermogel in solution
For low molecular weight triblock copolymers
PEG1000 can be used to slightly lower the gelation temperature

NaSCN can be used to raise the gelation temperature

Microarray nanoparticles

Microarray technology is a key factor in today's biotechnology research. There already exists a variety of chip-based polynucleic acids analysis systems. DNA microchips are already commercially available and are widely used in laboratories worldwide. In contrast, new methods are needed for the starting era of proteomics— the investigation of function, structure, and molecular interaction among proteins. Protein microarrays are widely expected to play an outstanding role in this new field of research.



To understand the flexibility of the practical approach of preparing nanoparticle-based microarrays, the overall process can be regarded as being composed of four different processes: 1) synthesis of functional nanoparticles;
2) Substrate surface activation step;
3) Nanoparticle deposition; and
4) Lithographic process.

Combining these processes in different ways provides the possibility to achieve the patterned deposition of nanoparticles in a direct or an indirect way. The performance of steps (2)-(4) will be described in "Surface Activation." Subsequently, we will introduce a selection of functional nanoparticles (step 1), which are designed to determine the surface chemistry of the resulting microarray. Finally, we will give an example of a microarray based on functional nanoparticles.

Nanoparticle Monolayer Array by Dip Coating of Nanoparticles on a Microstructured Activated Substrate

A microstructured activated surface can be used as a substrate for the microstructured deposition of particles by a simple dipping process. Therefore, subsequent to the photolithographic treatment, the chip is dipped in a nano-particle suspension, taken out, and simply rinsed with water. A microstructured nanoparticle array is thereby formed effectively. Fig. 3 shows a PDADMAC-pretreated and photolithographically patterned silica wafer after coating with silica nanoparticles. After the attachment of particles, a precise cutoff between the irradiated and non-irradiated sectors of the PDADMAC-coated silica surface was observed.

Nanoparticle Monolayer Array by Microspotting or Microcontact Printing on a Nonstructured Activated Substrate

For direct or mask-free structuring of nanoparticle layers, a drop of particle suspension is deposited by a microarrayer at a defined position of the surface (microspotting), or a patterned particle layer is transferred by means of an elastomeric stamp (microcontact printing).

After vaporescence of the liquid phase, the particles stay as a microstructured film at the initially homoge-nously coated

substrate. Examples for both routes are described in the following sections.

Microemulsion and durg delivery

The term "microemulsion" was first coined by Schulman et al. Microemulsions have attained significance in various sectors such as biotechnology, pharmaceuticals, analytical applications, food industries, cosmetics, agrochemicals, textiles, fuels, lubricants, enhanced oil recovery, environmental remediation and detoxification, and others. This could be explicated by their unique properties such as low interfacial tension, large surface area, thermodynamic stability and enhanced solubilization capacity.

Though microemulsions play a vital role in various fields, their importance in the field of pharmaceutics has significantly increased in recent years. This could be due to their ease of preparation at cost effective methods, high stability and optical transparency. Microemulsions act as potent drug delivery systems and they could be administered through various routes such as oral, parenteral, topical, ophthalmic and nasal routes. They also enable drug targeting, tumor targeting, brain targeting and cellular targeting. Microemulsions act as an excellent antibacterial, antifungal, antiviral and antitumor agent as well. A self-microemulsifying drug delivery system of curcumin showed improved aqueous solubility, oral bioavailability and high loading efficiency. The droplets were produced spontaneously in the nano range with minimum polydispersity. They demonstrated good cytostatic action against HeLa cells and also exhibited antibacterial activity against E. coli and S. aureus respectively. A clotrimazoleloaded H. suaveolens oil microemulsion gel demonstrated significant antifungal activity against against T. mentagrophyte, T. rubrum, M. gypseum and C. albicans as well. This carboxy methyl mungbean gel based formulation showed sustained release with improved penetration and antifungal property as compared to other available commercial forms. A recent study demonstrated that etoposide loaded coix seed oil microemulsion system with a droplet size of 35 nm induced apoptosis in A549 human lung carcinoma cells. Another study of olive oil-in-water emulsions preserved the viability of mycobacteria and showed positive response in bladder cancer treatment.

Nanocapsule

A nanocapsule is a nanoscale shell made from a nontoxic polymer. They are vesicular systems made of a polymeric membrane which encapsulates an inner liquid core at the nanoscale. Nanocapsules have many uses, including promising medical applications for drug delivery, food enhancement, nutraceuticals, and for self-healing materials. The benefits of encapsulation methods are for protection of these substances to protect in the adverse environment, for controlled release, and for precision targeting. Nanocapsules can potentially be used as MRI-guided nanorobots or nanobots, although challenges remain.

IUPAC definition

Hollow nanoparticle composed of a solid shell that surrounds a core-forming space available to entrap substances.

Structure

The typical size of the nanocapsule used for various applications ranges from 10-1000 nm. However, depending on the preparation and use of the nanocapsule, the size will be more specific.

Nanocapsule structure consists of nanovesicular system that is formed in a core-shell arrangement. The shell of a typical nanocapsule is made of a polymeric membrane or coating. The type of polymers used is of biodegradable polyester, as nanocapsules are often used in biological systems. Poly-e-caprolactone (PCL), poly(lactide) (PLA), and poly(lactide-co-glicolide) (PLGA) are typical polymers used in nanocapsule formation. Other polymers include thiolated poly(methacrylic acid) and poly(N-vinyl Pyrrolidone). As synthetic polymers have proven to be more pure and reproducible when compared naturally occurring polymers, they are often preferred for the construction nanocapsules.

However, some natural occurring polymers such as chitosan, gelatin, sodium alginate, and albumin are used in some drug delivering nanocapsules. Other nanocapsule shells include liposomes, along with polysaccharides and saccharides. Polysaccharides and saccharides are used due to their non-toxicity and biodegradability. They are attractive to use as they resemble biological membranes.

The core of a nanocapsule is composed of an oil surfactant that is specifically selected to coordinate with the selected drug within the polymeric membrane. The specific oil used must be highly soluble with the drug, and non-toxic when used in a biological environment. The oil-drug emulsion must have low solubility with the polymer membrane to ensure that the drug will be carried throughout the system properly and be released at the proper time and location. When the proper emulsion is obtained, the drug should be uniformly dispersed throughout the entire internal cavity of the polymeric membrane.

Processing

The encapsulation method depends on the requirements for any given drug or substance. These processes depend on the physiochemical properties of the core material, the wall material, and the required size. The most common ways to produce nanocapsules are nanoprecipitation, emulsion-diffusion, and solvent-evaporation.

In the nanoprecipitation method, also termed solvent displacement method, nanocapsules are formed by creating a colloidal suspension between two separate phases. The organic phase consists of a solution and a mixture of organic solvents. The aqueous phase consists of a mixture of non-solvents that forms a surface film. The organic phase is slowly injected in the aqueous phase which then is agitated to form the colloidal suspension. Once the colloidal suspension is formed it will be agitated until nanocapsules begin to form. The size and shape of the nanocapsule depend on the rate of injection along with the rate of agitation.

Another common way to prepare nanocapsules is the emulsion diffusion method. This method consists of three phases: organic, aqueous, and dilution phase. In this method the organic phase is added to the aqueous phase under conditions of high agitation which form an emulsion. During this process water is added to the emulsion which causes the solvent to diffuse. The result of this emulsion-diffusion is nanocapsule formation.

Solvent evaporation is another effective method to prepare nanocapsules. In this process, single or double emulsions are formed from solvents and are used to formulate a nanoparticle suspension. High speed homogenization or ultrasonication is used to form small particle size in the nanoparticle suspension. Once the suspension is stable, the solvents are evaporated using either continuous magnetic stirring at room temperature, or by reducing the ambient pressure.

Processing issues and solutions

Nanocapsules tend to aggregate and become unstable. Thus, substances within capsules can leak. To control the instability, nanocapsules can be dried either through spray drying or freeze-drying (lyophilization).

Spray drying – Solutions are sprayed into a drying medium. This method is more widely used in the food industry and used for encapsulation of many food products as flavors, minerals, colors, and vitamins. This method makes nanocapsules more stable, and increases shelf-life of foods.

Freeze-drying – This process involves dehydration of materials that are heat-sensitive. Unlike spray drying, water is removed through the sublimation process without changing the structure or shape of the

nanoparticles. Freeze-drying involves four states: freezing, primary drying, secondary drying, and storage. Because of the multiple stages involved, this method is considered to demand more energy and time

Properties

Absorbability: Aspect ratio affects the ability of the nanocapsule to penetrate tumor cells. Low aspect ratios (spherical capsules) tend to penetrate cells more easily than high aspect ratios (rod-shaped capsules).

Structure: The nano-sized structure of nanocapsules allows permeating through cell membranes, which makes them effective carriers of medicine in biological systems. The specific processing of nanocapsules gives them unique properties in how they release drugs in certain situations. Generally, there are three physico-chemical release mechanisms that are used to release the drug or medicine from the polymeric shell of the nanocapsule.

Delivery: Hydration and diffusion – In this release mechanism the nanocapsule will swell due to the effects of hydration. Once the nanocapsule has swollen to a point where it stretches, the polymeric membrane will allow for diffusion of the drug through the polymeric membrane and into the biological system.

Enzymatic reaction – The polymer shell must be first selected to coordinate with the enzymes produced by the human body to produce and enzymatic reaction. This reaction will cause a rupture in the polymeric membrane which allows the drug to be dispersed into the system.

Dissociation of the drug – The drug dissociates from the swelled nanocapsule and diffuses out into the rest of the cell.

Applications

Cancer: Water-soluble polymer shells are being created to deliver a protein, apoptin,[11] into cancer cells. The protein goes into the nucleus of the cancer cells while leaving healthy cells alone, unlike other conventional therapies as gene therapies and chemotherapy.[12] The capsules are 100 nm in size.

Active targeting of cancer cells is also being researched. Through active targeting, the nanocapsules form ligands that bind to malignant cells for cell delivery. This method is especially beneficial for those drugs that are not as permeable through the cell membrane, and where tissues are diseased, the nanoparticles are able to bond easier with the malignant cells.

Food usage: Nanoencapuslation in foods involves the changing of textures, flavorings, colorings, and stability in shelf-life.

Nutraceuticals: Nutraceuticals are substances that are placed in food to enhance nutrition. The increased bioavailability of these substances is relative to the size of the nanocarrier. The smaller the nanocarrier, the better the delivery properties and the solubility of the nutraceuticals; the nanocarrier is able to enter the bloodstream easier if smaller.

Ethyl alcohol absorption: Relatively new research involves the encapsulation of digestive enzymes within a non-toxic polymer shell. The enzyme filled nanoshell has been proven in lab mice to absorb ethyl alcohol from the bloodstream, therefore resulting in reduced blood alcohol levels. It has been concluded that the particles act as organelles, which proposes other benefits to enzyme therapies. This discovery is introducing other studies, such as encapsulation methods for hair loss.

Self-healing materials: For materials such as components in microelectronics, polymeric coatings, and adhesives, nanocapsules can reduce damage caused by high loads. The healing of cracks within these materials is alleviated by dispersing nanocapsules within the polymer. The healing substances include dicyclopentadiene (DCPD), which is prepared on site within the material by sonication. The nanoencapsulated material is first emulsified within the host material by creating an oil-in-water self-healing epoxy. The emulsified material is then agitated within the host material to form particles which then bond to the host material.

Nanomedicine

Nanomedicine is the medical application of nanotechnology. Nanomedicine ranges from the medical applications of nanomaterials and biological devices, to nanoelectronic biosensors, and even possible future applications of molecular nanotechnology such as biological machines. Current problems for nanomedicine involve understanding the issues related to toxicity and environmental impact of nanoscale materials (materials whose structure is on the scale of nanometers, i.e. billionths of a meter).

Functionalities can be added to nanomaterials by interfacing them with biological molecules or structures. The size of nanomaterials is similar to that of most biological molecules and structures; therefore, nanomaterials can be useful for both in vivo and in vitro biomedical research and applications. Thus far, the integration of nanomaterials with biology has led to the development of diagnostic devices, contrast agents, analytical tools, physical therapy applications, and drug delivery vehicles.

Drug delivery

Nanoparticles (top), liposomes (middle), and dendrimers (bottom) are some nanomaterials being investigated for use in nanomedicine.

Nanotechnology has provided the possibility of delivering drugs to specific cells using nanoparticles. The overall drug consumption and side-effects may be lowered significantly by depositing the active agent in the morbid region only and in no higher dose than needed. Targeted drug delivery is intended to reduce the side effects of drugs with concomitant decreases in consumption and treatment expenses. Drug delivery focuses on maximizing bioavailability both at specific places in the body and over a period of time. This can potentially be achieved by molecular targeting by nanoengineered devices. A benefit of using nanoscale for medical technologies is that smaller devices are less invasive and can possibly be implanted inside the body, plus biochemical reaction times are much shorter. These devices are faster and more sensitive than typical drug delivery.

The efficacy of drug delivery through nanomedicine is largely based upon:

a) Efficient encapsulation of the drugs,

b) Successful delivery of drug to the targeted region of the body, and

c) Successful release of the drug.

Applications: Some nanotechnology-based drugs that are commercially available or in human clinical trials include:

Abraxane, approved by the U.S. Food and Drug Administration (FDA) to treat breast cancer, non-small-cell lung cancer (NSCLC) and pancreatic cancer, is the nanoparticle albumin bound paclitaxel.

Doxil was originally approved by the FDA for the use on HIV-related Kaposi's sarcoma. It is now being used to also treat ovarian cancer and multiple myeloma. The drug is encased in liposomes, which helps to extend the life of the drug that is being distributed.

C-dots (Cornell dots) are the smallest silica-based nanoparticles with the size <10 nm. The particles are infused with organic dye which will light up with fluorescence.

Cancer

Nanoparticles have high surface area to volume ratio. This allows for many functional groups to be attached to a nanoparticle, which can seek out and bind to certain tumor cells. Additionally, the small size of nanoparticles (10 to 100 nanometers), allows them to preferentially accumulate at tumor sites (because tumors lack an effective lymphatic drainage system). Limitations to conventional cancer chemotherapy include drug resistance, lack of selectivity, and lack of solubility. Nanoparticles have the potential to overcome these problems.

In photodynamic therapy, a particle is placed within the body and is illuminated with light from the outside. The light gets absorbed by the particle and if the particle is metal, energy from the light will heat the particle and surrounding tissue. Light may also be used to produce high energy oxygen molecules which will chemically react with and destroy most organic molecules that are next to them (like tumors). This therapy is appealing for many reasons. It does not leave a "toxic trail" of reactive molecules throughout the body (chemotherapy) because it is directed where only the light is shined and the particles exist. Photodynamic therapy has potential for a noninvasive procedure for dealing with diseases, growth and tumors. Kanzius RF therapy is one example of such therapy (nanoparticle hyperthermia) .[citation needed] Also, gold nanoparticles have the potential to join numerous therapeutic functions into a single platform, by targeting specific tumor cells, tissues and organs.

Imaging

In vivo imaging is another area where tools and devices are being developed. Using nanoparticle contrast agents, images such as ultrasound and MRI have a favorable distribution and improved contrast. In cardiovascular imaging, nanoparticles have potential to aid visualization of blood pooling, ischemia, angiogenesis, atherosclerosis, and focal areas where inflammation is present.

The small size of nanoparticles endows them with properties that can be very useful in oncology, particularly in imaging. Quantum dots (nanoparticles with quantum confinement properties, such as size-tunable light emission), when used in conjunction with MRI (magnetic resonance imaging), can produce exceptional images of tumor sites. Nanoparticles of cadmium selenide (quantum dots) glow when exposed to ultraviolet light. When injected, they seep into cancer tumors. The surgeon can see the glowing tumor, and use it as a guide for more accurate tumor removal.These nanoparticles are much brighter than organic dyes and only need one light source for excitation. This means that the use of fluorescent quantum dots could produce a higher contrast image and at a lower cost than today's organic dyes used as contrast media. The downside, however, is that quantum dots are usually made of quite toxic elements, but this concern may be addressed by use of fluorescent dopants.

Tracking movement can help determine how well drugs are being distributed or how substances are metabolized. It is difficult to track a small group of cells throughout the body, so scientists used to dye the cells. These dyes needed to be excited by light of a certain wavelength in order for them to light up. While different color dyes absorb different frequencies of light, there was a need for as many light sources as cells. A way around this problem is with luminescent tags. These tags are quantum dots attached to proteins that penetrate cell membranes. The dots can be random in size, can be made of bio-inert material, and they demonstrate the nanoscale property that color is size-dependent. As a result, sizes are selected so that the frequency of light used to make a group of quantum dots fluoresce is an even multiple of the frequency required to make another group incandesce. Then both groups can be lit with a single light source. They have also found a way to insert nanoparticles into the affected parts of the body so that those parts of the body will glow showing the tumor growth or shrinkage or also organ trouble.

Sensing

Nanotechnology-on-a-chip is one more dimension of lab-on-a-chip technology. Magnetic nanoparticles, bound to a suitable antibody, are used to label specific molecules, structures or microorganisms. In particular silica nanoparticles are inert from the photophysical point of view and might accumulate a large number of dye(s) within the nanoparticle shell. Gold nanoparticles tagged with short segments of DNA can be used for detection of genetic sequence in a sample. Multicolor optical coding for biological assays has been achieved by embedding different-sized quantum dots into polymeric microbeads. Nanopore technology for analysis of nucleic acids converts strings of nucleotides directly into electronic signatures.

Sensor test chips containing thousands of nanowires, able to detect proteins and other biomarkers left behind by cancer cells, could enable the detection and diagnosis of cancer in the early stages from a few drops of a patient's blood. Nanotechnology is helping to advance the use of arthroscopes, which are pencil-sized devices that are used in surgeries with lights and cameras so surgeons can do the surgeries with smaller incisions. The smaller the incisions the faster the healing time which is better for the patients. It is also helping to find a way to make an arthroscope smaller than a strand of hair.

Research on nanoelectronics-based cancer diagnostics could lead to tests that can be done in pharmacies. The results promise to be highly accurate and the product promises to be inexpensive. They could take a very small amount of blood and detect cancer anywhere in the body in about five minutes, with a sensitivity that is a thousand times better than in a conventional laboratory test. These devices that are built with nanowires to detect cancer proteins; each nanowire detector is primed to be sensitive to a different cancer marker. The biggest advantage of the nanowire detectors is that they could test for anywhere from ten to one hundred similar medical conditions without adding cost to the testing device. Nanotechnology has also helped to personalize oncology for the detection, diagnosis, and treatment of cancer. It is now able to be tailored to each individual’s tumor for better performance. They have found ways that they will be able to target a specific part of the body that is being affected by cancer.

Blood purification

Magnetic micro particles are proven research instruments for the separation of cells and proteins from complex media. The technology is available under the name Magnetic-activated cell sorting or Dynabeads among others. More recently it was shown in animal models that magnetic nanoparticles can be used for the removal of various noxious compounds including toxins, pathogens, and proteins from whole blood in an extracorporeal circuit similar to dialysis. In contrast to dialysis, which works on the principle of the size related diffusion of solutes and ultrafiltration of fluid across a semi-permeable membrane, the purification with nanoparticles allows specific targeting of substances. Additionally larger compounds which are commonly not dialyzable can be removed.

The purification process is based on functionalized iron oxide or carbon coated metal nanoparticles with ferromagnetic or superparamagnetic properties. Binding agents such as proteins, antibodies, antibiotics, or synthetic ligands are covalently linked to the particle surface. These binding agents are able to interact with target species forming an agglomerate. Applying an external magnetic field gradient allows exerting a force on the nanoparticles. Hence the particles can be separated from the bulk fluid, thereby cleaning it from the contaminants.

The small size (< 100 nm) and large surface area of functionalized nanomagnets leads to advantageous properties compared to hemoperfusion, which is a clinically used technique for the purification of blood and is based on surface adsorption. These advantages are high loading and

accessibility of the binding agents, high selectivity towards the target compound, fast diffusion, small hydrodynamic resistance, and low dosage.

Tissue engineering

Nanotechnology may be used as part of tissue engineering to help reproduce or repair or reshape damaged tissue using suitable nanomaterial-based scaffolds and growth factors. Tissue engineering if successful may replace conventional treatments like organ transplants or artificial implants. Nanoparticles such as graphene, carbon nanotubes, molybdenum disulfide and tungsten disulfide are being used as reinforcing agents to fabricate mechanically strong biodegradable polymeric nanocomposites for bone tissue engineering applications. The addition of these nanoparticles in the polymer matrix at low concentrations (~0.2 weight %) leads to significant improvements in the compressive and flexural mechanical properties of polymeric nanocomposites. Potentially, these nanocomposites may be used as a novel, mechanically strong, light weight composite as bone implants.

For example, a flesh welder was demonstrated to fuse two pieces of chicken meat into a single piece using a suspension of gold-coated nanoshells activated by an infrared laser. This could be used to weld arteries during surgery. Another example is nanonephrology, the use of nanomedicine on the kidney.

Medical devices

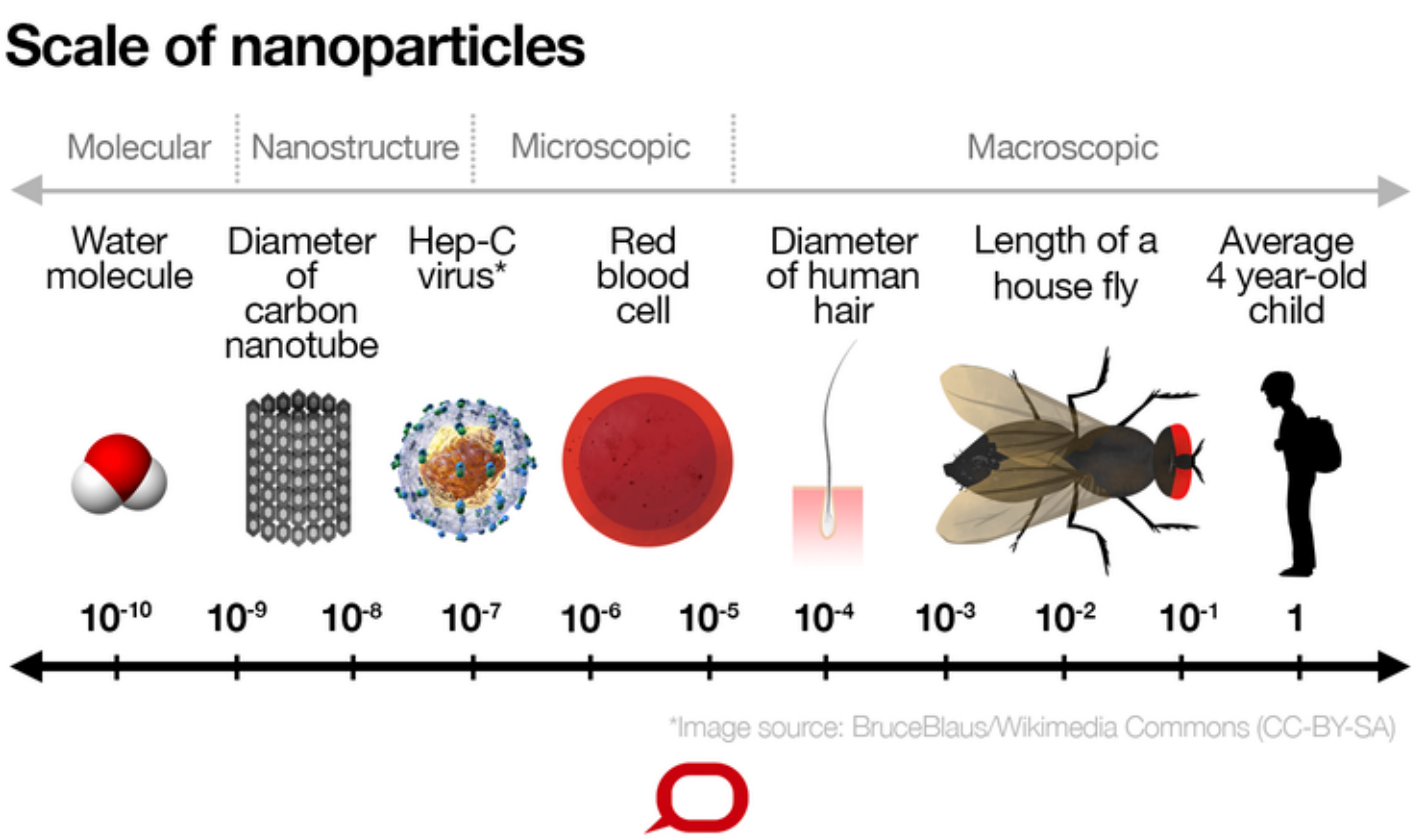
Neuro-electronic interfacing is a visionary goal dealing with the construction of nanodevices that will permit computers to be joined and linked to the nervous system. This idea requires the building of a molecular structure that will permit control and detection of nerve impulses by an external computer. A refuelable strategy implies energy is refilled continuously or periodically with external sonic, chemical, tethered, magnetic, or biological electrical sources, while a nonrefuelable strategy implies that all power is drawn from internal energy storage which would stop when all energy is drained. A nanoscale enzymatic biofuel cell for self-powered nanodevices have been developed that uses glucose from biofluids including human blood and watermelons. One limitation to this innovation is the fact that electrical interference or leakage or overheating from power consumption is possible. The wiring of the structure is extremely difficult because they must be positioned precisely in the nervous system. The structures that will provide the interface must also be compatible with the body's immune system.

Molecular nanotechnology is a speculative subfield of nanotechnology regarding the possibility of engineering molecular assemblers, machines which could re-order matter at a molecular or atomic scale. Nanomedicine would make use of these nanorobots, introduced into the body, to repair or detect damages and infections. Molecular nanotechnology is highly theoretical, seeking to anticipate what inventions nanotechnology might yield and to propose an agenda for future inquiry. The proposed elements of molecular nanotechnology, such as molecular assemblers and nanorobots are far beyond current capabilities. Future advances in nanomedicine could give rise to life extension through the repair of many processes thought to be responsible for aging.

What is nanomedicine?

Nanomedicine is the application of nanomaterials, or nanoparticles, to medicine. Nanoparticles are a form of transport for drugs and can go places drugs wouldn’t be able to go on their own.

Nanoparticles can be engineered and designed to package and transport drugs directly to where they’re needed. This targeted approach means the drugs cause most harm in the particular, and intended, area of the tumour they are delivered to. This minimises collateral damage to surrounding healthy tissues, and therefore the side effects.



The first cancer nanomedicine approved by the US Food and Drug Administration was Doxil. Since 1995, it has been used to treat adult cancers including ovarian cancer, multiple myeloma and Karposi's sarcoma (a rare cancer that often affects people with immune deficiency such as HIV and AIDS).

Currently, there is a stream of new nanomedicine treatments for adult cancers in clinical trials (trials in humans), or on the market. But only a limited number of these have been approved for children's cancers, although this is arguably where nanomedicine's strengths could have the most benefit.

How does nanomedicine work?

The nanoparticle drug-delivery systems can work in different ways. Along with carrying the drug for delivery, nanoparticles can be engineered to carry specific compounds that will let them bind, or attach, to molecules on tumour cells. Once attached, they can safety deliver the drug to the specific tumour site.

Nanoparticles can also help with drug solubility. For a drug to work, it must be able to enter the bloodstream, which means it needs to be soluble. For example, the cancer drug paclitaxel (Taxol) is insoluble so has to be dissolved in a delivery agent to get into the blood. But this agent can cause allergic reactions in patients.

To overcome these issues, chemists have developed a nanoparticle out of the naturally occurring protein albumin. It carries the paclitaxel and makes it soluble but without the allergic reactions.

Tumours commonly have disordered and leaky blood vessels sprouting through and off them. These vessels allow chemotherapy drugs to readily enter the tumour, but because chemotherapy molecules are so small, they also diffuse through the vessels and out of the tumour, attacking surrounding tissues. Nanoparticles are larger molecules that get trapped inside the tumour, where they do all the damage.

Once they have delivered their drug cargo to cells, nanoparticles can be designed to break down into harmless byproducts. This is particularly important for children who are still developing.

The term nanomedicine encompasses a broad range of technologies and materials. Types of nanomaterials that have been investigated for use as drugs, drug carriers or other nanomedicinal agents include:

- Dendrimers
- Polymers
- Liposomes
- Micelles
- Nanocapsules
- Nanoparticles
- Nanoemulsions

Around 250 nanomedicine products are being tested or used in humans, according to a new report that analyzed evolving trends in this sector. According to experts, the long-term impact of nanomedicinal products on human health and the environment is still not certain.

During the last 10 years, there has been steep growth in development of devices that integrate nanomaterials or other nanotechnology. Enhancement of in vivo imaging and testing has been a highly popular area of research, followed by bone substitutes and coatings for implanted devices.

Active and passive cell targeting will continue to be an important focus in nanomedicine. Targeted nano-enhanced solutions have been shown to often enhance existing treatments, and some nanomedicinal techniques are being developed which work as diagnosis and treatment stages simultaneously.

Implantable Biosensors

Micro-electromechanical systems (MEMS) and silicon chips that are capable of implantation within the human body may permit interfacing semiconductor devices with living tissues.

Implantable Glucose Sensors

A molecular nanotechnology company Zyvex, specializing in MEMS, chose Diabetech LP as its medical device commercialization and development partner for their wireless sensor implant targeting real-time blood glucose levels in the body. Their novel portable device for patients does not only display the glucose levels from the implant to the patient but also conveys automatically in real time the information to GlucoDynamix, the clinical management system of Diabetech.

Integration with Monitoring Systems

Virtual Medical World published an article in November 2005 that stated that a research project financed by the Academy of Finland was underway to develop of minute subcutaneous sensors that can be used for active monitoring of the heart or prosthetic joint function even over long time periods.

For instance, a subcutaneous EKG monitor can detect cardiac arrhythmia, and this data can be wirelessly transmitted to the PC or mobile phone of the physician.

Chronic Disease Monitoring

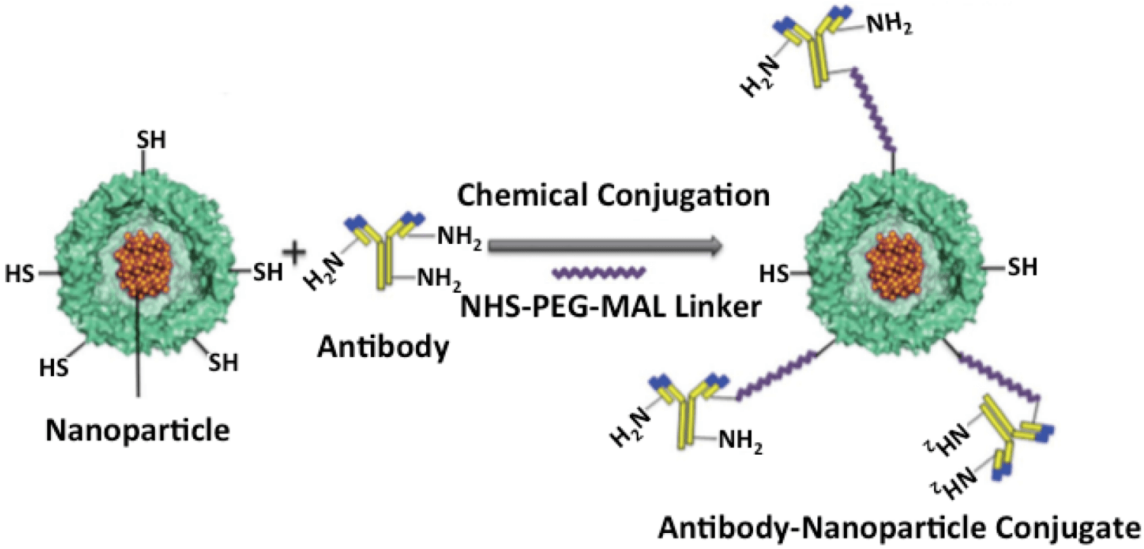
Guidant is a specialist in treating vascular and cardiac disease and has invested in CardioMEMS based on an article published in Virtual Medical Worlds in November, 2005. CardioMEMS develops novel devices based on MEMS technology to help physicians monitor remotely the progress of chronic diseases like heart failure.

The nano pressure sensor can monitor pressure within the cardiovascular system while the data is transmitted to a wristwatch-like data collection device. The data is transmitted by this external device to a central remote monitoring station where it can be seen by health care providers in real time.

Antibody-Nanoparticle Probes

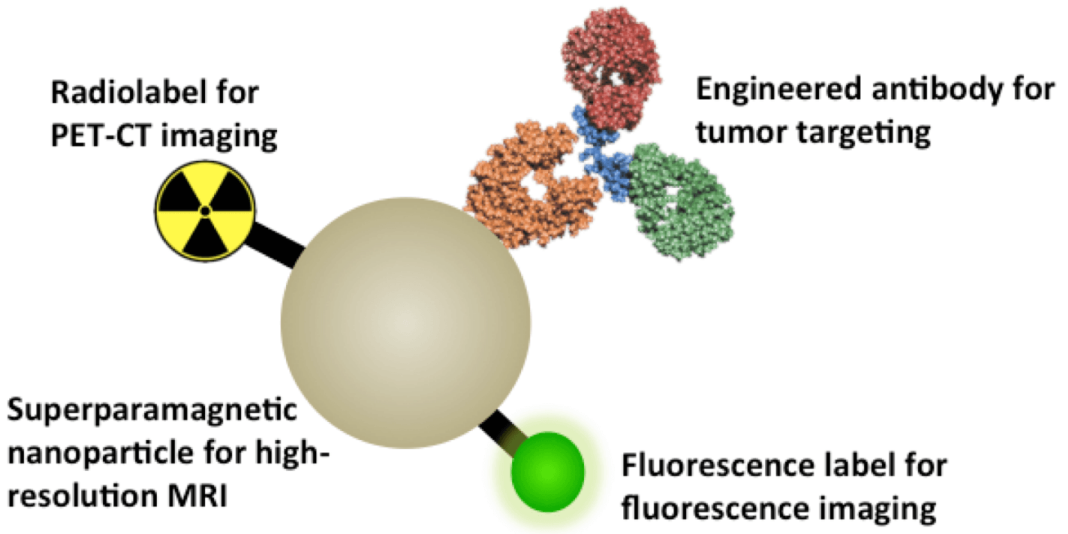
Nanoparticles have been widely investigated and exploited for decades in a broad range of biomedical studies and applications. With sizes in the nano-scale range (10-100 nm), nanoparticles are perfect candidates as probes or drug-carriers for high-resolution imagery, efficient diagnosis, and drug delivery vesicles. Many therapies involving nanoparticles have been developed for numerous diseases including cancer, diabetes and Alzheimer's disease. With the development of biochemical and biomedical technologies, nanoparticles have become controllable in size, shape, composition, and properties for a variety of applications. For instance, gold nanoparticle (Au NP) is an attractive contrast provider for the visualization of biomaterials with a number of different techniques, including optical microscopy, electron microscopy, photothermal imaging, and photoacoustic imaging. With more sophisticatedly optimized physicochemical properties, Au NPs are also chosen as high-resolution X-ray imaging contrast agents for the diagnosis and analysis of tumor-related diseases.

Advances in nano-biotechnology in the past few decades have enabled a series of strategies for nanoparticle modification and optimization. The most commonly used strategies are the attachment or conjugation of different functional groups, moieties or ligands to the surface of nanoparticles. Antibodies and their derivatives, among a broad range of targeting ligands, have been shown to efficiently direct the nanoparticles as imaging agents, nano-probes or drug carriers, to their desired sites in the body. Comparing to the free nanoparticles, antibody-conjugated nanoparticles are more site-specific, resulting in higher accumulation on the target area and consequently, lower dosage requirements. Since nanoparticles can be synthesized or post-synthetically modified with diverse surface groups, it is convenient to conjugate the nanoparticles with antibodies either by using a short linker or via direct interactions through different chemical reactions (thio-maleimide reaction, amine-carboxyl reaction…) or bio-recognitions (avidin-biotin interaction…).



An example of antibody-nanoparticle conjugation via chemical reactions using a polyethylene glycol (PEG) based linker (*Nanoscale*, 2013).

An example of a custom antibody-nanoparticle probe: the multi-functionalized superparamagnetic nanoparticle can be used as the contrast agent for high-resolution MRI; the radiolabel on the nanoparticle makes the nanoparticle detectable by using PET/CT imaging techniques; the fluorescence label provides the nanoparticle with the ability to be detected by fluorescence imaging techniques; the antibody conjugated with the nanoparticle is able to efficiently direct the nanoparticle to specific tumor sites in the body, which enables the antibody-nanoparticle probe to be used for high-resolution imagery and the diagnosis of cancer with the help of different techniques.



Earlier Detection and Diagnosis

In the fight against cancer, half of the battle is won based on its early detection. Nanotechnology provides new molecular contrast agents and materials to enable earlier and more accurate initial diagnosis as well as in continual monitoring of cancer patient treatment.

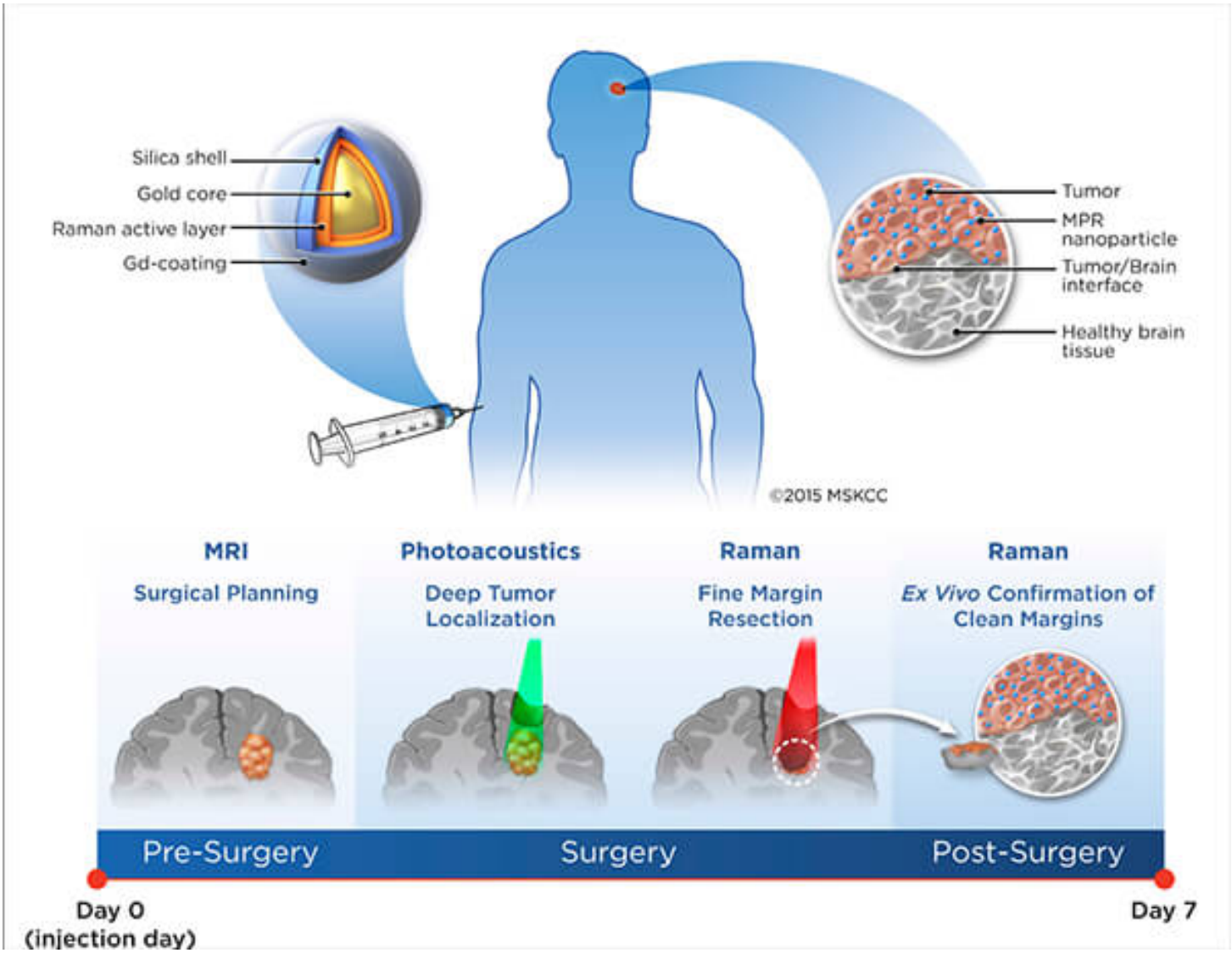
Already clinically established as contrast agents for anatomical structure, nanoparticles are being developed to act as molecular imaging agents, reporting on the presence of cancer-relevant genetic mutations or the functional characteristics of tumor cells. This information can be used to choose a treatment course or alter a therapeutic plan. Bioactivatable nanoparticles that change properties in response to factors or processes within the body act as dynamic reporters of in vivo states and can provide both spatial and temporal information on disease progression and therapeutic response.

Imaging *In Vivo*

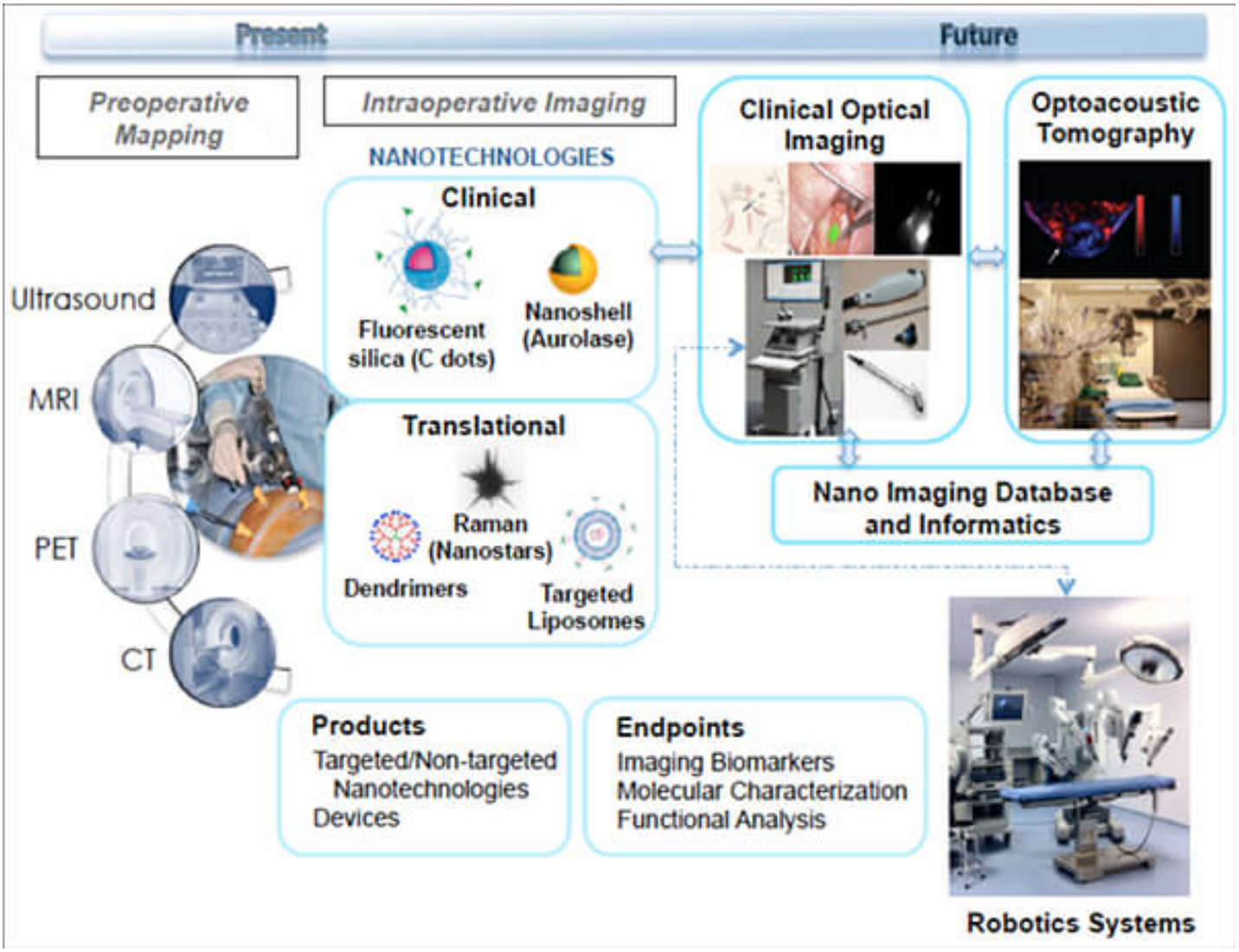
Current imaging methods can only detect cancers once they have made a visible change to a tissue, by which time, thousands of cells will have proliferated and perhaps metastasized. And even when visible, the nature of the tumor—malignant or benign—and the characteristics that might make it responsive to a particular treatment must be assessed through tissue biopsies. Furthermore, while some primary malignancies can be determined to be metastatic, tumor pre-seeding of metastatic sites and micro-metastases are extremely difficult to detect with modern imaging modalities, even if the tissue in which they commonly occur are known, *a priori*. Finally, surgical resection of tumor tissue remains the standard of care for many tumor types and surgeons must weigh the consequences of removing often vital healthy tissue versus the cancerous mass which has grown non-uniformly within. Ultimately, removal of cancer cells at the single cell level is not possible with current surgical techniques.

Principle of a triple-modality MRI-photoacoustic-Raman nanoparticle for clinical use. The nanoparticle is injected intravenously. In contrast to small molecule contrast agents that wash out of the tumor quickly, the nanoparticles are stably internalized within the brain tumor cells, allowing the whole spectrum from preoperative MRI for surgical planning to intraoperative imaging to be performed with a single injection. T1-weighted MRI depicts the outline of the tumor due to the T1-shortening effect of the gadolinium. During the surgery, photoacoustic imaging with its greater depth penetration and 3D imaging capabilities can be used to guide the gross resection steps, while Raman imaging can guide the resection of the microscopic tumor at the resection margins. Raman would be used for rapid conformation of clean margins in the operating room instead of the time-consuming analysis of frozen

sections.



Present and future of NanoOncology Image-guided Surgical Suite. Preoperative conventional imaging tools are used to screen for disease and inform optically- driven minimally-invasive and open surgical procedures. Clinically available particle platforms can be monitored in real-time using portable multichannel camera systems. Representative translational probes and devices for future clinical use are also shown. In the future, the operating surgeon will select suitable probe-device combinations for specific indications, and be provided with structural, functional, and/or molecular-level data regarding ssue status for further treatment management.



Sensing In Vitro

Nanotechnology-enabled **in vitro diagnostic devices** offer high sensitivity and selectivity, and capability to perform simultaneous measurements of multiple targets. Well-established fabrication techniques (e.g., lithography) can be used to manufacture integrated, portable devices or point-of-care systems. A diagnostic device or biosensor contains a biological recognition element, which through biochemical reaction can detect the presence, activity or concentration of a specific biological molecule in the solution. This reaction could be associated, for example with: binding of antigen and antibody, hybridization of two single stranded DNA fragments, or binding of capture ligand to the cell surface epitope. A transducer part of the detection device is used to convert the biochemical event into a quantifiable signal which can be measured. The transduction mechanisms can rely on light, magnetic, or electronic effects.

Several devices have been designed for detection of various biological signatures from serum or tissue. Few examples of diagnostic devices relying on nanotechnology or nanoparticles are given in Figure #. The bio-barcode assay was designed as a sandwich immunoassay in the laboratory of Chad Mirkin at Northwestern University. It utilizes magnetic nanoparticles (MMPs) which are functionalized with monoclonal antibodies specific to the target protein of interest and then mixed with the sample to promote capture of target proteins. The MMP-protein hybrid structures are then combined with gold nanoparticle (Au-NP) probes which carry DNA-barcodes. Target protein-specific DNA barcodes are released into solution and detected using the scanometric assay with sensitivities in femto-picomolar range.

Measuring Response to Therapy and the Liquid Biopsy

Measurement of an individual patient's response to therapeutics during the course of their disease is the basis for precise and prognostic medical care. Accurate and disease relevant monitoring can allow for optimized treatment regimens (e.g., therapeutic course correction, drug combinations, and dose attenuation), preemptive clinical decision making (e.g., therapeutic responders vs. non-responders, and more), and patient stratification for clinical trials. Beyond the more traditional gold standards of in vivo imaging, tissue biopsy and in vitro diagnostics available for this purpose, the "liquid biopsy" offers the ability to measure response to therapy by way of simple and serial blood draws. Traditional biopsies involve resection of small volumes of the tumor tissue directly, and thus, remain invasive procedures that cannot offer the sampling necessitated to track disease progression relative to the course of therapy or the dynamics of its evolving biology. Liquid biopsies rely on the fact that tumors shed material (e.g., cells, DNA, other cancer-specific biomolecules) into circulation, over time and in response to therapy. Although, the amount of materials shed by any given tumor and / or stage is typically at incredibly low concentrations relative to the rest of the blood's constituents (e.g., erythrocytes, leukocytes, thrombocytes, plasma, etc.). This requires specific and sensitive tools to detect, capture, and purify the circulating tumor material relative to the rest. Nanotechnology is enabling these tools to become reality.

Recent technological advances in the coupling of complex microfluidics and nanoscale materials have allowed the high-purity capture and downstream functional characterization of circulating tumor cells (CTCs), cell-free tumor DNA, microemboli, exosomes, proteins, neoantigens, and more. Recent examples include, capture and subsequent release of CTCs within microfluidic systems to maintain viable cells for downstream whole genome sequencing, ex vivo expansion, RNA sequencing, and more. Of these examples, one type of device uses magnetic nanoparticles to enrich whole blood prior to magnetic separation within the microfluidic and the other device uses thermoresponsive nanopolymers that specifically capture CTCs as they flow through the microfluidic then release upon a change in temperature once blood processing is complete. In both cases, the detection sensitivities are very high (e.g., for enumeration >95%) and capture purity is much higher than other non-nanomaterial based devices. Furthermore, the processing times are increasing every year as the technology evolves, currently averaging 10 mL blood per 30 minutes.

Treatment and Therapy

Cancer therapies are currently limited to surgery, radiation, and chemotherapy. All three methods risk damage to normal tissues or incomplete eradication of the cancer. Nanotechnology offers the means to target chemotherapies directly and selectively to cancerous cells and neoplasms, guide in surgical resection of tumors, and enhance the therapeutic efficacy of radiation-based and other current treatment modalities. All of this can add up to a decreased risk to the patient and an increased probability of survival.

Research on nanotechnology cancer therapy extends beyond drug delivery into the creation of new therapeutics available only through use of nanomaterial properties. Although small compared to cells, nanoparticles are large enough to encapsulate many small molecule compounds, which can be of multiple types. At the same time, the relatively large surface area of nanoparticle can be functionalized with ligands, including small molecules, DNA or RNA strands, peptides, aptamers or antibodies. These ligands can be used for therapeutic effect or to direct nanoparticle fate in vivo. These properties enable combination drug delivery, multi-modality treatment and combined therapeutic and diagnostic, known as "theranostic," action. The physical properties of nanoparticles, such as energy absorption and re-radiation, can also be used to disrupt diseased tissue, as in laser ablation and hyperthermia applications. Integrated development of innovative nanoparticle packages and active pharmaceutical ingredients will also enable exploration of a wider repertoire of active ingredients, no longer confined to those with acceptable pharmokinetic or biocompatibility behavior. In addition, immunogenic cargo and surface coatings are being investigated as both adjuvants to nanoparticle-mediated and traditional radio- and

chemotherapy as well as stand-alone therapies. Innovative strategies include the design of nanoparticles as artificial antigen presenting cells and in vivo depots of immunostimulatory factors that exploit nanostructured architecture for sustained anti-tumor activity.

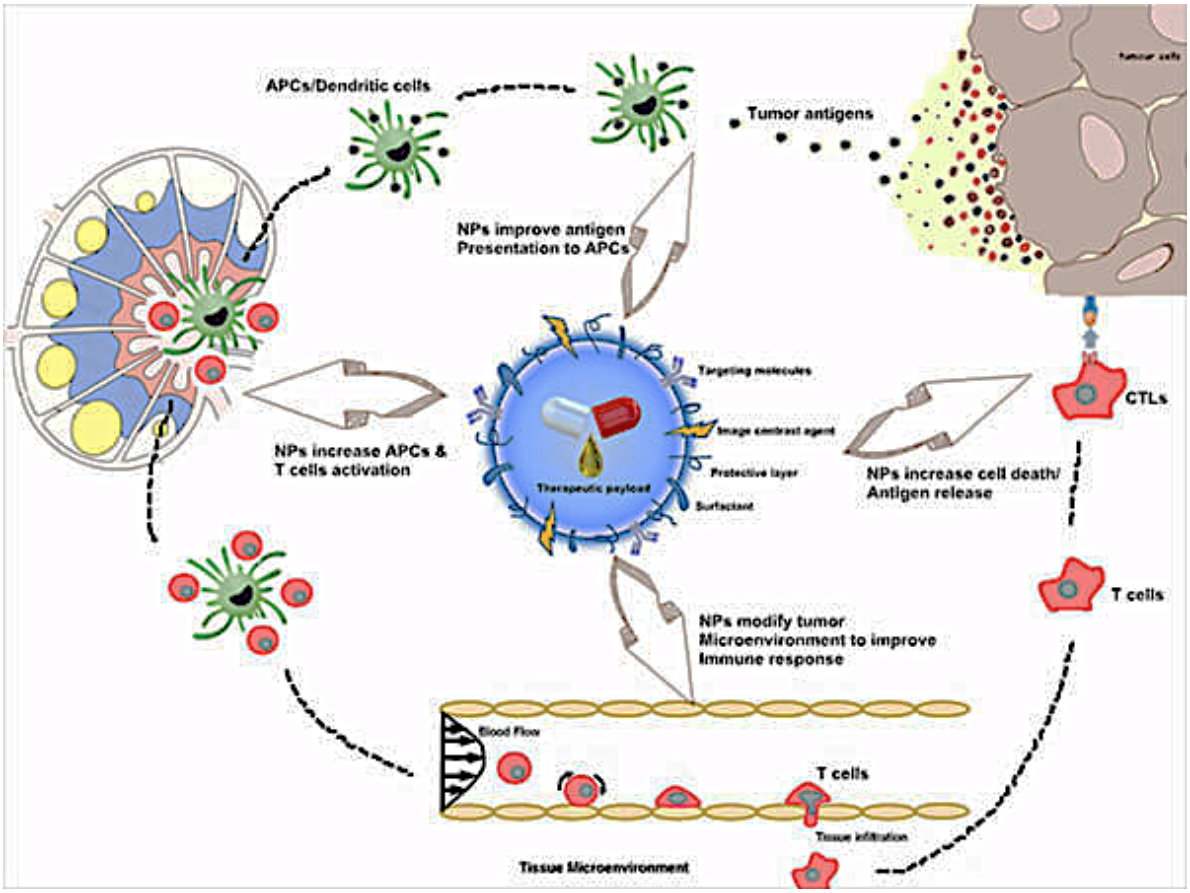
Delivering Chemotherapy

The traditional use of nanotechnology in cancer therapeutics has been to improve the pharmacokinetics and reduce the systemic toxicities of chemotherapies through the selective targeting and delivery of these anticancer drugs to tumor tissues. The advantage of nanosized carriers is that they can increase the delivered drug's overall therapeutic index through nanoformulations in with chemotherapeutics are either encapsulated or conjugated to the surfaces of nanoparticles. This capability is largely due to their tunable size and surface properties. Size is a major factor in the delivery of nanotechnology-based therapeutics to tumor tissues. Selective delivery of nanotherapeutic platforms depends primarily on the passive targeting of tumors through the enhanced permeability and retention (EPR) effect. This phenomenon relies on defects specific to tumor microenvironment such as defects in lymphatic drainage, along with increased tumor vasculature permeability, to allow nanoparticles (<200 nm) to accumulate in the tumor microenvironment. Furthermore, the timing or site of drug release can be controlled by triggered events, such as ultrasound, pH, heat, or by material composition.

Nano-enabled Immunotherapy

Immunotherapy is a promising new front in cancer treatment encompassing a number of approaches, including checkpoint inhibition and cellular therapies. Although results for some patients have been spectacular, only a minority of patients being treated for just a subset of cancers experience durable responses to these therapies. Expanding the benefits of immunotherapy requires a greater understanding of tumor-host immune system interactions. New technologies for molecular and functional analysis of single cells are being used to interrogate tumor and immune cells and elucidate molecular indicators and functional immune responses to therapy. To this end, nano-enabled devices and materials are being leveraged to sort, image, and characterize T cells in the Alliance's NanoSystems Biology Cancer Center.

Nanotechnologies are also being investigated to deliver immunotherapy. This includes use of nanoparticles for delivery of immunostimulatory or immunomodulatory molecules in combination with chemo- or radiotherapy or as adjuvants to other immunotherapies. Standalone nanoparticle vaccines are also being designed to raise sufficient T cell response to eradicate tumors, through co-delivery of antigen and adjuvant, the inclusion of multiple antigens to stimulate multiple dendritic cell targets, and continuous release of antigens for prolonged immune stimulation. Molecular blockers of immune-suppressive factors produced can also be co-encapsulated in nanoparticle vaccines to alter the immune context of tumors and improve response, an approach being pursued in the Nano Approaches to Modulate Host Cell Response for Cancer Therapy Center at UNC. Researchers in this Center are also investigating the use of nanoparticles to capture antigens from tumors following radiotherapy to create patient specific treatments, similar in principle to a "dendritic cell activating scaffold" currently in a Phase I clinical trial.



Depiction of the complex pathway involved in cancer immunotherapy. Nanoparticle delivery vehicles can play a role at multiple points along this pathway.

Delivering or Augmenting Radiotherapy

Roughly half of all cancer patients receive some form of radiation therapy over the course of their treatment. Radiation therapy uses high-energy radiation to shrink tumors and kill cancer cells. Radiation therapy kills cancer cells by damaging their DNA inducing cellular apoptosis. Radiation therapy can either damage DNA directly or create charged particles (atoms with an odd or unpaired number of electrons) within the cells that can in turn damage the DNA. Most types of radiation used for cancer treatment utilize X-rays, gamma rays, and charged particles. As such, they are inherently toxic to all cells, not just cancer cells, and are given in doses that are as efficacious as possible while not being too harmful to the body or fatal. Because of this tradeoff between efficacy and safety relative to tumor type, location, and stage, often the efficacy of treatment must remain at reduced levels in order to not be overtly toxic to surrounding tissue or organs near the tumor mass.

Delivering Gene Therapy

The value of nanomaterial-based delivery has become apparent for new types of therapeutics such as those using nucleic acids, which are highly unstable in systemic circulation and sensitive to degradation. These include DNA and RNA-based genetic therapeutics such as small interfering RNAs (siRNAs), and microRNAs (miRNAs). Gene silencing therapeutics, siRNAs, have been reported to have significantly extended half-lives when delivered either encapsulated or conjugated to the surface of nanoparticles. These therapeutics are used in many cases to target 'undruggable' cancer proteins. Additionally, the increased stability of genetic therapies delivered by nanocarriers, and often combined with controlled release, has been shown to prolong their effects.

Nanoremediation

Nanoremediation is the use of nanoparticles for environmental remediation. It is being explored to treat ground water, wastewater, soil, sediment, or other contaminated environmental materials. Nanoremediation is an emerging industry; by 2009, nanoremediation technologies had been documented in at least 44 cleanup sites around the world, predominantly in the United States. In Europe, nanoremediation is being investigated by the EC funded NanoRem Project. A report produced by the NanoRem consortium has identified around 70 nanoremediation projects worldwide at pilot or full scale. During nanoremediation, a nanoparticle agent must be brought into contact with the target contaminant under conditions that allow a detoxifying or immobilizing reaction. This process typically involves a pump-and-treat process or *in situ* application.

Some nanoremediation methods, particularly the use of nano zero-valent iron for groundwater cleanup, have been deployed at full-scale cleanup sites. Other methods remain in research phases.

Applications

Nanoremediation has been most widely used for groundwater treatment, with additional extensive research in wastewater treatment. Nanoremediation has also been tested for soil and sediment cleanup. Even more preliminary research is exploring the use of nanoparticles to remove toxic materials from gases.

Groundwater remediation

Currently, groundwater remediation is the most common commercial application of nanoremediation technologies. Using nanomaterials, especially zero-valent metals (ZVMs), for groundwater remediation is an emerging approach that is promising due to the availability and effectiveness of many nanomaterials for degrading or sequestering contaminants.

Nanotechnology offers the potential to effectively treat contaminants *in situ*, avoiding excavation or the need to pump contaminated water out of the ground. The process begins with nanoparticles being injected into a contaminated aquifer via an injection well. The nanoparticles are then transported by groundwater flow to the source of contamination. Upon contact, nanoparticles can sequester contaminants (via adsorption or complexation), immobilizing them, or they can degrade the contaminants to less harmful compounds. Contaminant transformations are typically redox reactions. When the nanoparticle is the oxidant or reductant, it is considered reactive.

The ability to inject nanoparticles to the subsurface and transport them to the contaminant source is imperative for successful treatment. Reactive nanoparticles can be injected into a well where they will then be transported down gradient to the contaminated area. Drilling and packing a well is quite expensive. Direct push wells cost less than drilled wells and are the most often used delivery tool for remediation with nanoiron. A nanoparticle slurry can be injected along the vertical range of the probe to provide treatment to specific aquifer regions.

Surface water treatment

The use of various nanomaterials, including carbon nanotubes and TiO_2, shows promise for treatment of surface water, including for purification, disinfection, and desalination. Target contaminants in surface waters include heavy metals, organic contaminants, and pathogens. In this context, nanoparticles may be used as sorbents, as reactive agents (photocatalysts or redox agents), or in membranes used for nanofiltration.

Trace contaminant detection

Nanoparticles may assist in detecting trace levels of contaminants in field settings, contributing to effective remediation. Instruments that can operate outside of a laboratory often are not sensitive enough to detect trace contaminants. Rapid, portable, and cost-effective measurement systems for trace contaminants in groundwater and other environmental media would thus enhance contaminant detection and cleanup. One potential method is to separate the analyte from the sample and concentrate them to a smaller volume, easing detection and measurement. When small quantities of solid sorbents are used to absorb the target for concentration, this method is referred to as solid-phase microextraction.

With their high reactivity and large surface area, nanoparticles may be effective sorbents to help concentrate target contaminants for solid-phase microextraction, particularly in the form of self-assembled monolayers on mesoporous supports. The mesoporous silica structure, made through a surfactant templated sol-gel process, gives these self-assembled monolayers high surface area and a rigid open pore structure. This material may be an effective sorbent for many targets, including heavy metals such as mercury, lead, and cadmium, chromate and arsenate, and radionuclides such as ^{99}Tc, ^{137}CS, uranium, and the actinides.

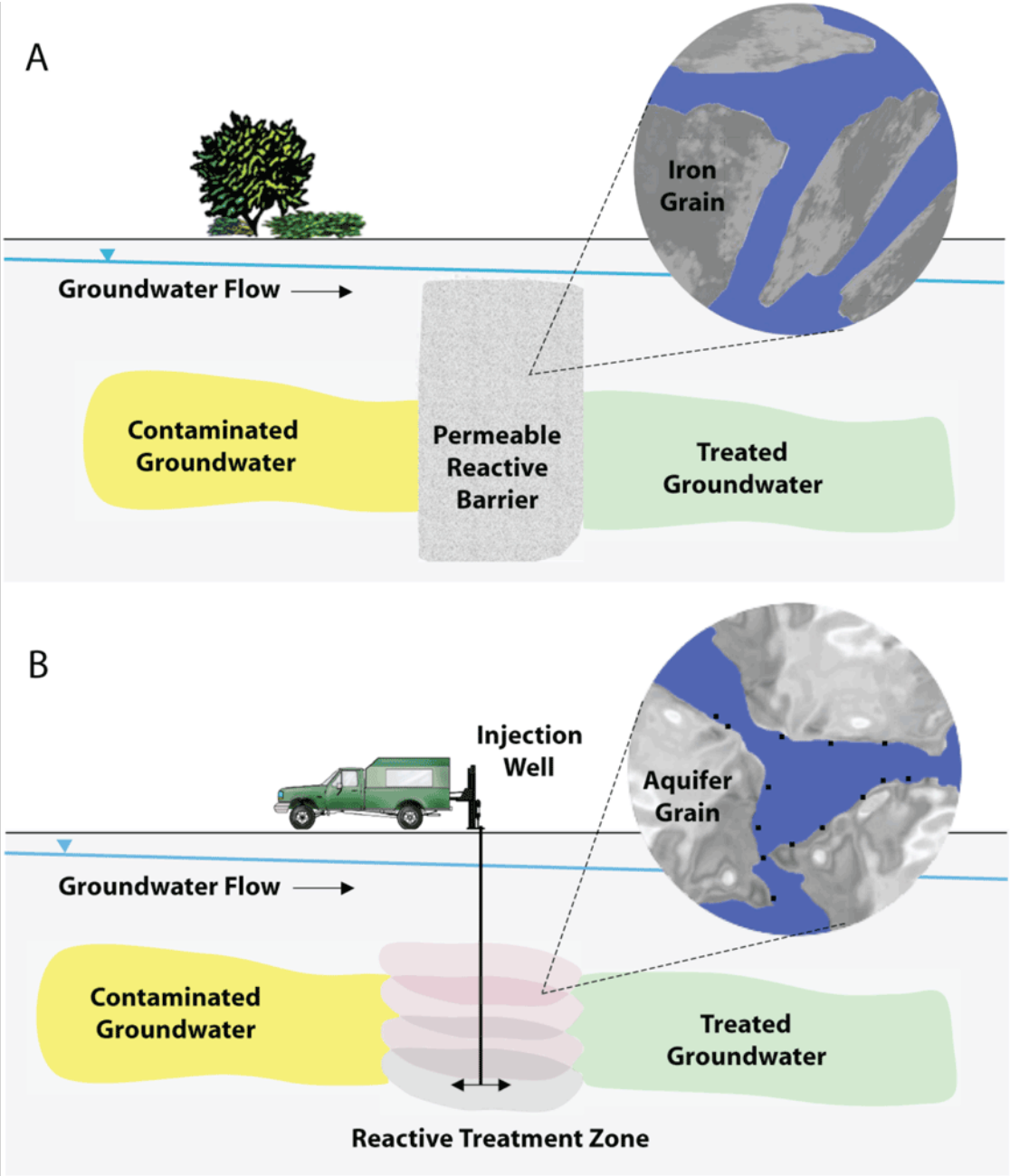


Figure 4 illustrates the basic principles of two methods of remediating contaminated groundwater using nZVI. The image at the top shows treatment of DNAPL contamination by injection of nanoscale materials. In the second image, a reactive treatment zone is formed by a series of injections of nZVI. These injections create overlapping zones of particles that become lodged within the native aquifer material.

Nanofiltration

Nanofiltration (NF) is a relatively recent membrane filtration process used most often with low

total dissolved solids water such as surface water and fresh groundwater, with the purpose of softening (polyvalent cation removal) and removal of disinfection by-product precursors such as natural organic matter and synthetic organic matter.

Nanofiltration is also becoming more widely used in food processing applications such as dairy, for simultaneous concentration and partial (monovalent ion) demineralisation.

Overview

Nanofiltration is a membrane filtration-based method that uses nanometer sized through-pores that pass through the membrane. Nanofiltration membranes have pore sizes from 1-10 nanometers, smaller than that used in microfiltration and ultrafiltration, but just larger than that in reverse osmosis. Membranes used are predominantly created from polymer thin films. Materials that are commonly used include polyethylene terephthalate or metals such as aluminum. Pore dimensions are controlled by pH, temperature and time during development with pore densities ranging from 1 to 106 pores per cm^2. Membranes made from polyethylene terephthalate and other similar materials, are referred to as "track-etch" membranes, named after the way the pores on the membranes are made. "Tracking" involves bombarding the polymer thin film with high energy particles. This results in making tracks that are chemically developed into the membrane, or "etched" into the membrane, which are the pores. Membranes created from metal such as alumina membranes, are made by electrochemically growing a thin layer of aluminum oxide from aluminum metal in an acidic medium.

Range of applications

Historically, nanofiltration and other membrane technology used for molecular separation was applied entirely on aqueous systems. The original uses for nanofiltration were water treatment and in particular water softening. Nanofilters can "soften" water by retaining scale-forming, hydrated divalent ions (e.g. Ca^{2+}, Mg^{2+}) while passing smaller hydrated monovalent ions.

In recent years, the use of nanofiltration has been extended into other industries such as milk and juice production. Research and development in solvent-stable membranes has allowed the application for nanofiltration membranes to extend into new areas such as pharmaceuticals, fine chemicals, and flavour and fragrance industries. Development in organic solvent nanofiltration technology and commercialization of membranes used has extended possibilities for applications in a variety of organic solvents ranging from non-polar through polar to polar aprotic.

Industry	Uses
Fine chemistry and Pharmaceuticals	Non-thermal solvent recovery and management Room temperature solvent exchange
Oil and Petroleum chemistry	Removal of tar components in feed Purification of gas condensates
Bulk Chemistry	Product Polishing Continuous recovery of homogeneous catalysts
Natural Essential Oils and similar products	Fractionation of crude extracts Enrichment of natural compounds Gentle Separations
Medicine	Able to extract amino acids and lipids from blood and other cell culture.

Advantages and disadvantages

One of the main advantages of nanofiltration as a method of softening water is that during the process of retaining calcium and magnesium ions while passing smaller hydrated monovalent ions, filtration is performed without adding extra sodium ions, as used in ion exchangers.[8] Many separation processes do not operate at room temperature (e.g. distillation), which greatly increases the cost of the process when continuous heating or cooling is applied. Performing gentle molecular separation is linked

with nanofiltration that is often not included with other forms of separation processes (centrifugation). These are two of the main benefits that are associated with nanofiltration. Nanofiltration has a very favorable benefit of being able to process large volumes and continuously produce streams of products. Still, Nanofiltration is the least used method of membrane filtration in industry as the membrane pores sizes are limited to only a few nanometers. Anything smaller, reverse osmosis is used and anything larger is used for ultrafiltration. Ultrafiltration can also be used in cases where nanofiltration can be used, due to it being more conventional. A main disadvantage associated with nanotechnology, as with all membrane filter technology, is the cost and maintenance of the membranes used. Nanofiltration membranes are an expensive part of the process. Repairs and replacement of membranes is dependent on total dissolved solids, flow rate and components of the feed. With nanofiltration being used across various industries, only an estimation of replacement frequency can be used. This causes nanofilters to be replaced a short time before or after their prime usage is complete.

Design and operation

Industrial applications of membranes require hundreds to thousands of square meters of membranes and therefore an efficient way to reduce the footprint by packing them is required. Membranes first became commercially viable when low cost methods of housing in 'modules' were achieved. Membranes are not self-supporting. They need to be stayed by a porous support that can withstand the pressures required to operate the NF membrane without hindering the performance of the membrane. To do this effectively, the module needs to provide a channel to remove the membrane permeation and provide appropriate flow condition that reduces the phenomena of concentration polarisation. A good design minimises pressure losses on both the feed side and permeate side and thus energy requirements. Leakage of the feed into the permeate stream must also be prevented. This can be done through either the use of permanent seals such as glue or replaceable seals such as O-rings.

Concentration polarisation

Concentration polarisation describes the accumulation of the species being retained close to the surface of the membrane which reduces separation capabilities. It occurs because the particles are convected towards the membrane with the solvent and its magnitude is the balance between this convection caused by solvent flux and the particle transport away from the membrane due to the concentration gradient (predominantly caused by diffusion.) Although concentration polarisation is easily reversible, it can lead to fouling of the membrane.

Spiral wound module

Spiral wound modules are the most commonly used style of module and are 'standardized' design, available in a range of standard diameters (2.5", 4" and 8") to fit standard pressure vessel that can hold several modules in series connected by O-rings. The module uses flat sheets wrapped around a central tube. The membranes are glued along three edges over a permeate spacer to form 'leaves'. The permeate spacer supports the membrane and conducts the permeate to the central permeate tube. Between each leaf, a mesh like feed spacer is inserted. The reason for the mesh like dimension of the spacer is to provide a hydrodynamic environment near the surface of the membrane that discourages concentration polarisation. Once the leaves have been wound around the central tube, the module is wrapped in a casing layer and caps placed on the end of the cylinder to prevent 'telescoping' that can occur in high flow rate and pressure conditions.

Tubular module

Tubular modules look similar to shell and tube heat exchangers with bundles of tubes with the active surface of the membrane on the inside. Flow through the tubes is normally turbulent, ensuring low concentration polarisation but also increasing energy costs. The tubes can either be self-supporting or supported by insertion into perforated metal tubes. This module design is limited for nanofiltration by

the pressure they can withstand before bursting, limiting the maximum flux possible. Due to both the high energy operating costs of turbulent flow and the limiting burst pressure, tubular modules are more suited to 'dirty' applications where feeds have particulates such as filtering raw water to gain potable water in the Fyne process. The membranes can be easily cleaned through a 'pigging' technique with foam balls are squeezed through the tubes, scouring the caked deposits.

Flux enhancing strategies

These strategies work to reduce the magnitude of concentration polarisation and fouling. There is a range of techniques available however the most common is feed channel spacers as described in spiral wound modules. All of the strategies work by increasing eddies and generating a high shear in the flow near the membrane surface. Some of these strategies include vibrating the membrane, rotating the membrane, having a rotor disk above the membrane, pulsing the feed flow rate and introducing gas bubbling close to the surface of the membrane.

Characterisation

Many different factors must be taken into account in the design of NF membranes, since they vary so much in material, separation mechanisms, morphology and thus application. Two important parameters should be investigated during preliminary calculations, performance and morphology parameters.

Performance parameters

Retention of both charged and uncharged solutes and permeation measurements can be categorised into performance parameters since the performance under natural conditions of a membrane is based on the ratio of solute retained/ permeated through the membrane.

For charged solutes, the ionic distribution of salts near the membrane-solution interface plays an important role in determining the retention characteristic of a membrane. If the charge of the membrane and the composition and concentration of the solution to be filtered is known, the distribution of various salts can be found. This in turn can be combined with the known charge of the membrane and the Gibbs–Donnan effect to predict the retention characteristics for that membrane.

Uncharged solutes cannot be characterised simply by Molecular Weight Cut Off (MWCO,) although in general an increase in molecular weight or solute size leads to an increase in retention. The valence charge, chemical structure, functional end-groups as well as pH of the solute, all play an important role in determining the retention characteristics and as such detailed information about the solute molecule characteristics must be known before implementing a NF design.

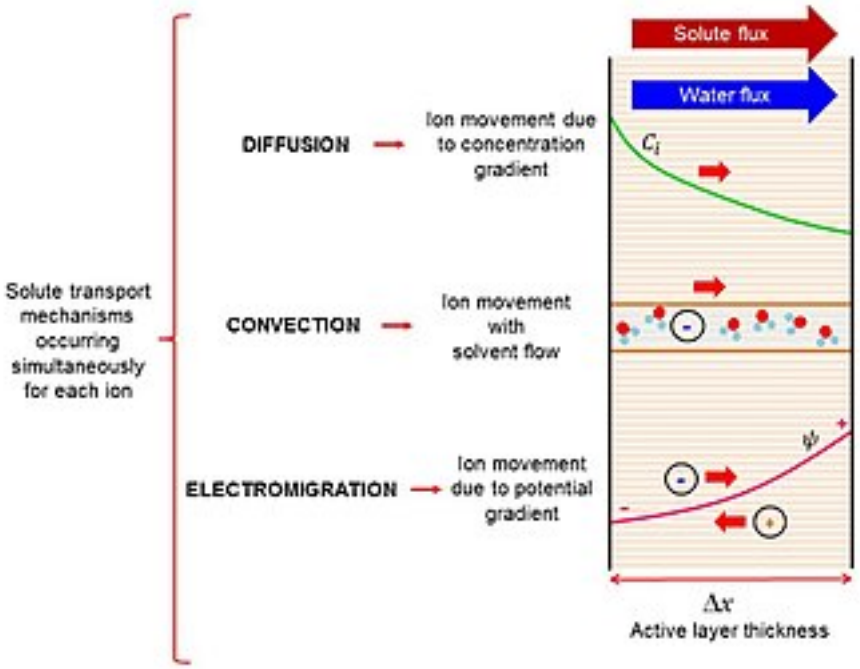
Morphology parameters

The morphology of a membrane must also be known in order to implement a successful design of a NF system, and this is usually done by microscopy. Atomic force microscopy (AFM) is one method used to characterise the surface roughness of a membrane by passing a small sharp tip (<100 Ă) across the surface of a membrane and measuring the resulting Van der Waals force between the atoms in the end of the tip and the surface. This is useful as a direct correlation between surface roughness and colloidal fouling has been developed. Correlations also exist between fouling and other morphology parameters, such as hydrophobe, showing that the more hydrophobic a membrane is, the less prone to fouling it is. See membrane fouling for more information.

Methods to determine the porosity of porous membranes have also been found via permporometry, making use of differing vapour pressures to characterise the pore size and pore size distribution within the membrane. Initially all pores in the membrane are completely filled with a liquid and as such no permeation of a gas occurs, but after reducing the relative vapour pressure some gaps will start to form within the pores as dictated by the Kelvin equation. Polymeric (non-porous) membranes cannot be subjected to this methodology as the condensable vapour should have a negligible interaction

within the membrane.

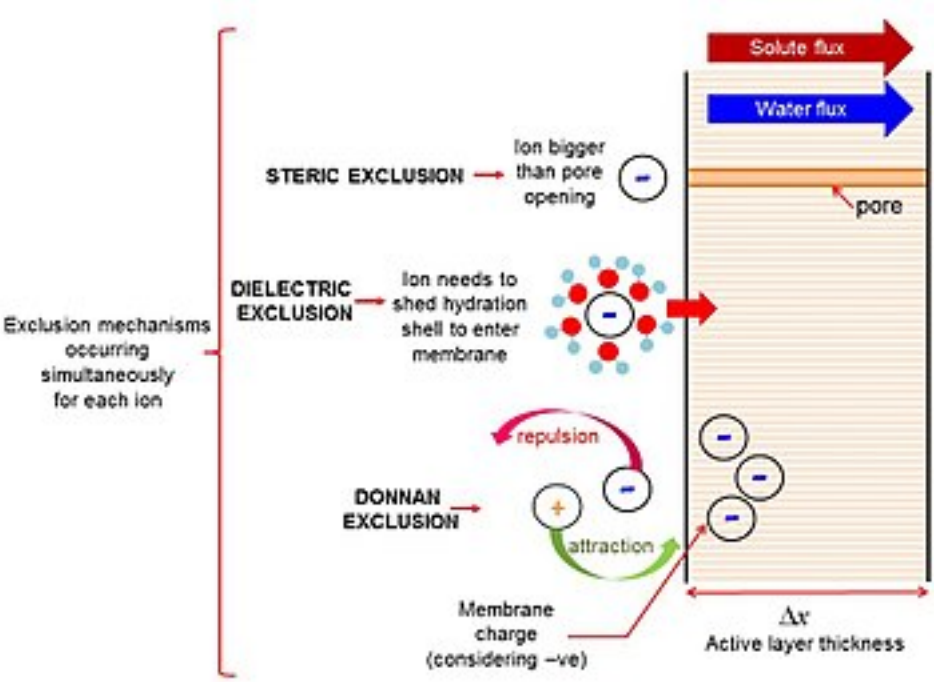
Solute transport and rejection



Mechanisms through which solutes in nanofiltration transport through the membrane.

Unlike membranes with larger and smaller poor sizes, passage of solutes through nanofiltration is significantly more complex. Because of the pore sizes, there are three modes of transport of solutes through the membrane. These include 1) diffusion (molecule travel due to concentration potential gradients, as seen through reverse osmosis membranes), 2) convection (travel with flow, like in larger pore size filtration such as microfiltration), and 3) electromigration (attraction or repulsion from charges within and near the membrane).

Additionally, the exclusion mechanisms in nanofiltration are more complex than in other forms of filtration. Most filtration systems operate solely by size (steric) exclusion, but at small length scales seen in nanofiltration, one must also consider the impacts of surface charge on the small charged solutes, and also the impacts of hydration, where molecules in solution have a solvation shell of surrounding water molecules. The exclusion due to hydration is referred to as dielectric exclusion, a reference to the different dielectric constants (energy) associated with a particles precense in solution



versus within a membrane substrate.

The transport and exclusion mechanisms are heavily influenced by membrane pore size, solvent viscosity, membrane thickness, solute diffusivity, solution temperature, solution pH, and membrane dielectric constant. The pore size distribution is also important. Modeling rejection accurately for NF is very challenging. It can be done with applications of the Nernst–Planck equation, although a heavy reliance on fitting parameters to experimental data is usually requried.

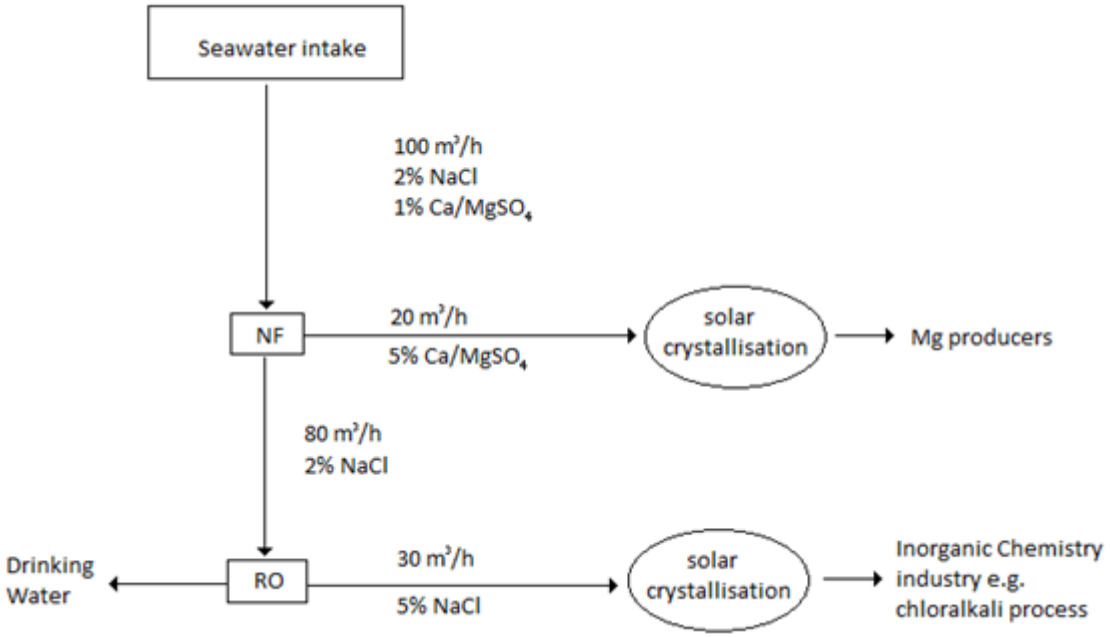
In general, charged solutes are much more effectively rejected in NF than uncharged solutes, and multivalent solutes like SO2− 4 (valence of 2) experience very high rejection.

Typical figures for industrial applications

Keeping in mind that NF is usually part of a composite system for purification, a single unit is chosen based off the design specifications for the NF unit. For drinking water purification many commercial membranes exist, coming from different chemical families, having different structures, chemical tolerances and salt rejections and so the characterisation must be chosen based on the chemical composition and concentration of the feed stream.

NF units in drinking water purification range from extremely low salt rejection (<5% in 1001A membranes) to almost complete rejection (99% in 8040-TS80-TSA membranes.) Flow rates range from 25–60 m^3/day for each unit, so commercial filtration requires multiple NF units in parallel to process large quantities of feed water. The pressures required in these units are generally between 4.5-7.5 bar.[11]

For seawater desalination using a NF-RO system a typical process is shown below.



Because of the fact that NF permeate is rarely clean enough to be used as the final product for drinking water and other water purification, is it commonly used as a pre treatment step for reverse osmosis (RO) as is shown above.

Post-treatment

As with other membrane based separations such as ultrafiltration, microfiltration and reverse osmosis, post-treatment of eitherpermeate or retentate flow streams (depending on the application) – is a necessary stage in industrial NF separation prior to commercial distribution of the product. The choice

and order of unit operations employed in post-treatment is dependent on water quality regulations and the design of the NF system. Typical NF water purification post-treatment stages include aeration and disinfection & stabilisation.

Aeration

A Polyvinyl chloride (PVC) or fibre-reinforced plastic (FRP) degasifier is used to remove dissolved gases such as carbon dioxide and hydrogen sulfide from the permeate stream. This is achieved by blowing air in a countercurrent direction to the water falling through packing material in the degasifier. The air effectively strips the unwanted gases from the water.

Disinfection and stabilisation

The permeate water from a NF separation is demineralised and may be disposed to large changes in pH, thus providing a substantial risk of corrosion in piping and other equipment components. To increase the stability of the water, chemical addition of alkaline solutions such as lime and caustic soda is employed. Furthermore, disinfectants such as chlorine or chloroamine are added to the permeate, as well as phosphate or fluoride corrosion inhibitors in some cases.

New developments

Contemporary research in the area of Nanofiltration (NF) technology is primarily concerned with improving the performance of NF membranes, minimising membrane fouling and reducing energy requirements of already existing processes. One way in which researchers are attempting to improve NF performance – more specifically increase permeate flux and lower membrane resistance – is through experimentation with different membrane materials and configurations. thin film composite membranes (TFC), which consist of a number of extremely thin selective layers interfacially polymerized over a microporous substrate, have had the most commercial success in industrial membrane applications due to the capability of optimizing the selectivity and permeability of each individual layer. Recent research has shown that the addition of nanotechnology materials such as electrospunnanofibrous membrane layers (ENMs) to conventional TFC membranes results in an enhanced permeate flux. This has been attributed to inherent properties of ENMs that favour flux, namely their interconnected pore structure, high porosity and low transmembrane pressure. A recently developed membrane configuration which offers a more energy efficient alternative to the commonly used spiral wound arrangement is the hollow fibre membrane. This format has the advantage of requiring significantly less pre-treatment than spiral wound membranes, as solids introduced in the feed are displaced effectively during backwash or flushing. As a result, membrane fouling and pre-treatment energy costs are reduced. Extensive research has also been conducted on the potential use of Titanium Dioxide (TiO2, titania) nanoparticles for membrane fouling reduction. This method involves applying a nonporous coating of titania onto the membrane surface. Internal fouling/pore blockage of the membrane is resisted due to the nonporosity of the coating, whilst the superhydrophilic nature of titania provides resistance to surface fouling by reducing adhesion of emulsified oil on the membrane surface.